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COMPLETE TEARS OF THE PERINEUM

PREPARATION, OPERATIVE TECHNIQUE, AND TREATMENT AFTER OPERATION

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A SURPRISINGLY large number of failures continue to occur in the management of complete or so-called third degree tears involving the rectovaginal septum and the sphincter ani muscles. These failures are due in some part to the technique used and again to the neglect of apparent trifles in the treatment after operation for repair.

Complete laceration of the female perineum is a subject as old as the beginnings of gynecology and one that frequently has been described and discussed. The earliest account that we find of an operation for a completely ruptured perineum is by Trotula, renowned woman physician and teacher of the School of Salerno in the eleventh century. The uterus, if prolapsed, must, she directed, be softened by hot wine compresses and replaced and the tear itself at once sutured. A tampon soaked in hot wine and butter was to be placed in the vagina, to retain the uterus, while deep stitches were to be taken at the anus, and in three or four other places, with silk thread, and the whole was to be well dusted with powder. Then a linen cloth soaked in tar water was to be tightly bandaged against the wound, and the patient's feet held "higher than the head." She was to be kept in this position for eight or nine days without bathing. She was not to be allowed to vomit, and her diet was to be very simple. Knowing, of course, nothing of sepsis, Trotula yet directed that pads were to be placed against the anus, or in the rectum, to prevent any contact with feces. But Trotula sensibly concludes: "Although the perineum will be stronger than before it was torn, it would have been better to avoid such injury by greater care at the birth of the baby."

During the eight hundred years since Trotula's book on gynecology was written, interest in complete perineal injuries has had many re-

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vivals. Techniques and treatments of various sorts have been introduced with the usual tilts between the reactionaries and the radicals. However, in recent years there has been a marked dearth of literature on repair and the end results of complete tears of the perineum. This may be due to the fact that too much is taken for granted or it may be that confusion still exists. But the fact is that failures do continue to occur, many of which could be avoided.

The operation for repair is one that requires the most meticulous and delicate surgical procedure and the most cautious and painstaking postoperative treatment, an operation depending upon these two factors and to some extent upon the degree of preoperative preparation. In the year 1873, when Thomas Addis Emmet apologized for harping on so old a subject as this, he started a new era for the technique for repair of the pelvic floor. At that time he remarked that for years his attention had been occupied with trying to unravel the cause of failure in uniting the torn sphincter ani muscles and to devise some means of obviating this failure, adding that "to appreciate so simple an explanation has cost me more thought than any other point in the whole field of the branch of surgery to which I have devoted myself."

The late C. Jeff Miller remarked shortly before his death in 1936 that he did not know of any condition in which more failures occurred than this. The sixty-three cases in the present series are from his services at Charity Hospital and Touro Infirmary, in New Orleans, during the years 1931 to 1935 inclusive and from my personal cases from 1931 to 1938.

TABLE I

	CHARITY HOSPITAL	TOURO INFIRMARY	TOTAL
1931	3	3	6
1932	4	7	11
1933	7	2	9
1934	13	5	18
1935	3	7	10
1936	3	2	5
1937	2	2	4
	35	28	63

There is a prevailing belief that improved obstetrics has greatly lessened the incidence of complete perineal lacerations. This point is debatable. The loss of sphincter ani muscle control is not always caused by faulty obstetrics. In two cases in this series loss of anal sphincter control resulted from accidental removal of segments of these muscles during previous hemorrhoidectomies. One case in this series, a girl 10 years of age, was the result of rape. The history, however, of the majority of patients with complete tears of the perineum reveals the

cause of obstetric injury sometimes as recent as two or three years, and more often dating back as far as ten, fifteen, and even twenty-nine years.

Incontinence of gaseous and fecal contents may or may not be an immediate result of perineal laceration. Some patients in this group reported a gradual loss of control extending over several years and a great number had endured complete absence of sphincter control over even a longer period of time. Diarrhea may develop after a long period as a result of complete perineal tears and frequently this symptom is the first complaint of the patient. It is always a matter of astonishment that so many women endure such a depressing and unsupportable condition to seek relief only when the acute stage of pain and discomfort is reached.

Uniform preparation and aftertreatment and, with a few exceptions, the same operative treatment were carried out in all the cases in the present series of sixty-three patients operated upon during the last seven years. The final results of the operations performed by Miller and by myself are given in Table II.

TABLE II*

	CHARITY HOSPITAL	TOURO INFIRMARY	TOTAL	PERCENTAGE
Perfect control	25	24	49	86%
Partial control	3	4	7	12%
Failure	0	2	2	2%
No information upon final result	2	3	5	
	—	—	—	
	30	33	63	

*Failure in one of the cases was due to the patient's having been given an enema the day following operation contrary to our direct instructions. This points out the necessity for the house staff and nursing service to follow definite orders as to the postoperative care of these patients.

Preparation Before Operation.—The three main objects of any measure taken in the preoperative preparation of patients with third degree lacerations of the perineum are to insure evacuation of the bowels, to facilitate maintenance of constipation for several days after operation, and, as nearly as possible, to guarantee a sterile operative field.

Hospitalization as a rule is not feasible until the day prior to operation. After admission to the hospital, liquids only are allowed. Treatment should begin twenty-four hours before operation when a dose of castor oil is given and only liquids by mouth are permitted until the time of operation. As an additional routine measure, an olive-oil and glycerin enema and a lysol douche are given in the early morning of the operative day. When the patient is under anesthesia in the operating room, the parts are thoroughly cleansed with soap and water and the field is irrigated.

I do not favor spinal anesthesia because it produces too much relaxation of the tissues. After reuniting the severed muscles under spinal anesthesia, the muscle tone is lost and the surgeon is unable to determine

whether or not the severed ends have been approximated. Therefore, some form of inhalation anesthesia is advised.

Should the patient be hospitalized earlier than the day before operation, preparatory measures are to start upon admission. Miller advised a series of high irrigations of the bowel and cleansing douches several days prior to operation. The patient should remain in bed during this period and a nonresidue diet should be maintained. The more thoroughly the preoperative treatment is directed toward evacuation of the

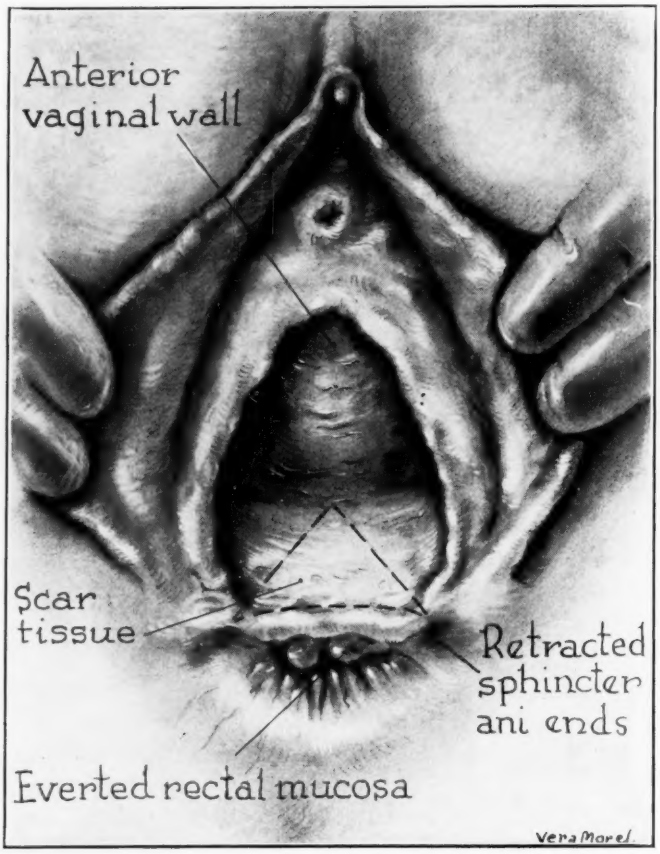

Fig. 1.—Showing complete tear of the perineum with excessive amount of scar tissue in the rectovaginal septum. The rectus mucosa is everted. The pits or depressions caused by the retraction of the sphincter ani muscles may be observed.

bowels and pre[illegible]cing constipation, so much easier will it be to prevent defecation after operation, until the desired number of days, and to avoid consequent contamination of the field and any strain upon the sutures. When care is taken to provide a mechanically sterile field, there is less danger of infection from sloughing and formation of stitch abscesses that may become rectovaginal fistulas.

In all cases in the present series this preoperative routine was followed and with but a few exceptions the patients were hospitalized on the day

preceding operation. In no case were there more than two or three days of hospitalization previous to operation.

Technique of Operation.—Injury is always a variable factor. The choice of operative closure must depend upon the extent of damage to the structures involved. The final test of any procedure is its adaptability to the individual case and whether or not its use will effect restoration of sphincter control.

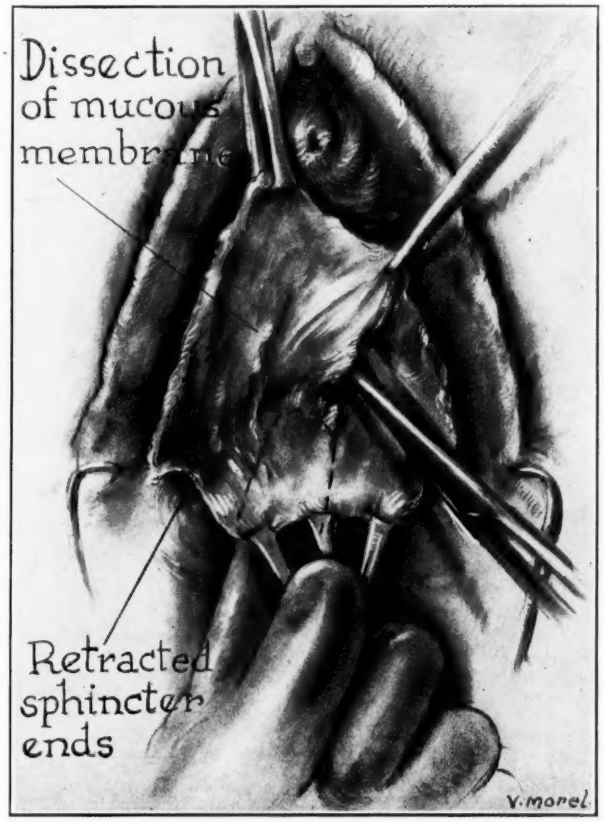

Fig. 2.—Mucous membrane is carefully dissected with scissors. Index finger is inserted into the rectum to facilitate the freeing of the mucous membrane from the scar tissue, also as a protection for the anterior wall of the rectum. A Gelpi self-retaining retractor is used throughout the operation.

When lacerations have existed for many years and considerable atrophic change has taken place in the sphincter ani muscles, fascia lata grafts, as recommended by Harvey Stone, or Sistrunk's method of uniting the ends of the torn sphincter ani muscles with the levator ani muscles will give almost perfect results. Ristine and Noble's operation is usually successful when the injury lies above the anal orifice. As in the Emmet or the Hegar perineorrhaphy, the anterior portion of the rectum is widely separated from the vaginal structures and the freed bowel is drawn down until the tear lies outside the sphincter ring.

Sutures may be inserted in this position, after which the sphincter ends are united and the usual perineorrhaphy is followed. The important advantage in this technique is that a line of suture does not remain in the rectovaginal septum. The operation, however, is applicable only to tears that do not extend high into the rectal wall. It is quite surprising how easily the bowel may be slid downward after free dissection and this technique is preferred to the Warren or the Farrar operation which necessitates the creation of a flap, or apron, from the vagina. This apron frequently will slough off because of circulation disturbances and an inexperienced operator by chance may "buttonhole" the flap in his dissection when such a tedious method is followed.

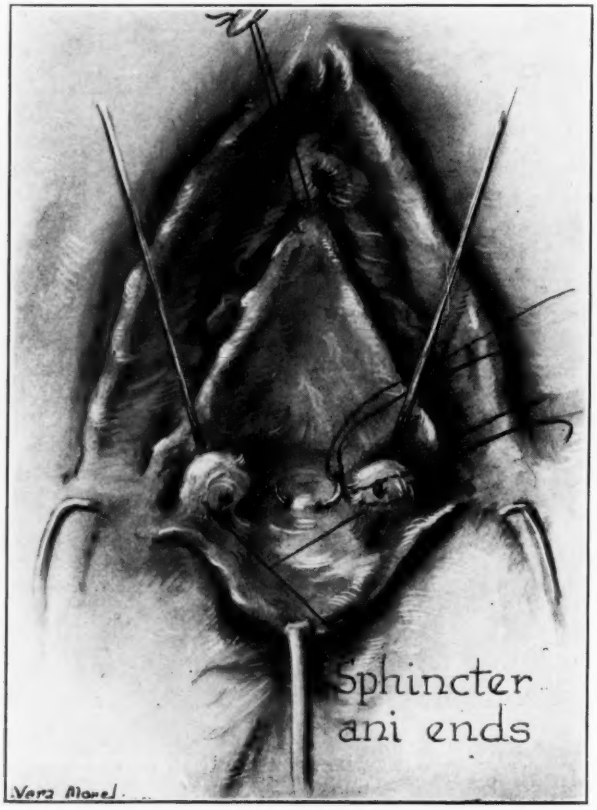

Fig. 3.—After careful dissection of the mucous membrane, allowing the rectal wall to be pulled down, the torn ends of the sphincter ani muscles are located by probing with hooks. A chromic No. 1 suture through the torn sphincter ani muscle ends is passed through the muscularis layer only of the rectal wall. This prevents retraction of the rectal wall above the reunited sphincter.

When the injury extends high within the rectum, or when there is an excessive amount of scar tissue to prevent mobilization, as is necessary in the Ristine-Noble procedure, the rectum and the vagina are separated as in the first steps of a perinorrhaphy. The tear in the rectal wall then is closed by a layer of fine linen sutures within the bowel and inverted (as is done with a Lembert intestinal suture) by a second layer of

chromic catgut sutures placed and tied on the vaginal side. After the sphincter ends are dissected and reunited, the perineal tear is repaired. This operation is the choice when the tear is recent and it is almost invariably the ideal technique for the majority of old lacerations.

The following precautions should be observed no matter what technique is followed: (1) free dissection and excision of all scar tissue; (2) sutures inserted to allow for swelling and to guarantee freedom from tension along the suture line. Quite often, after the sutures have been tied, it appears as though so much tension might interfere with the blood supply. The danger is usually from too much blood supply rather than from not enough so that after the sutures are tied we often make small, so-called "pie-crust" incisions, through the superficial skin layers of the perineum to permit the escape of ooze. This treatment proves of great value in the presence of edema or of tension.

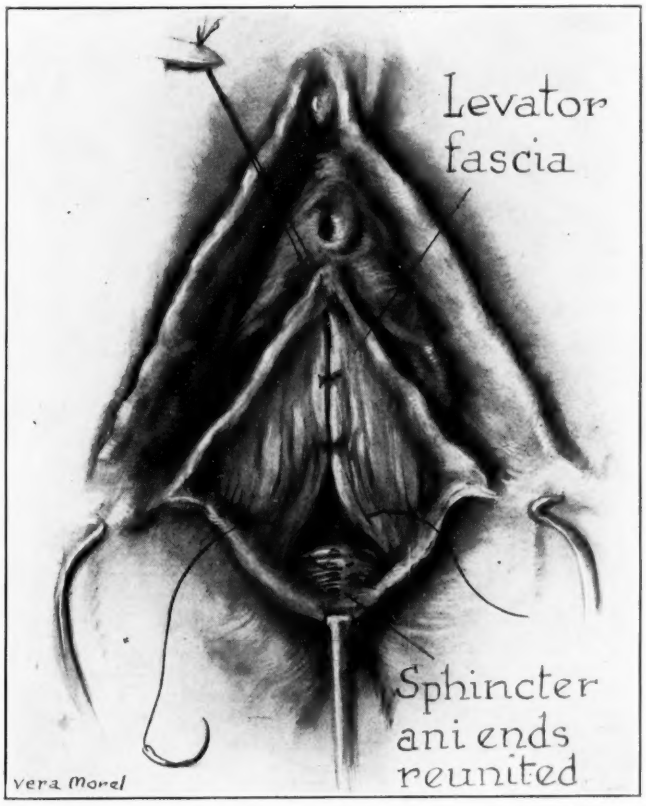

Fig. 4.—The sphincter ani ends have been reunited and the levator fascia and muscle are now closed with interrupted chromic No. 1 sutures. The last suture is passed through the reunited sphincter ani muscle.

Dead spaces are to be carefully avoided. After insertion of the final catgut sutures, four or more silkworm-gut sutures are placed from the perineal side to act as a splint should the catgut sutures break down from too much tension. The lowest suture passes through the ends of

the restored sphincter. The ends of these silkworm-gut sutures are gathered together at the top of the perineal wound and tied into one bunch by the topmost suture. In this way postoperative cleansing of the wound is simplified.

Chromic No. 1 catgut was used throughout this series of cases for uniting the ends of the sphincter ani and the levator ani muscles. Silkworm sutures were used to supplement these. When necessary to suture a tear in the rectum, fine linen was used with interrupted sutures and the ends tied within the rectum. No special dressing is required. The application of a simple perineal pad offers ample protection of the wound.

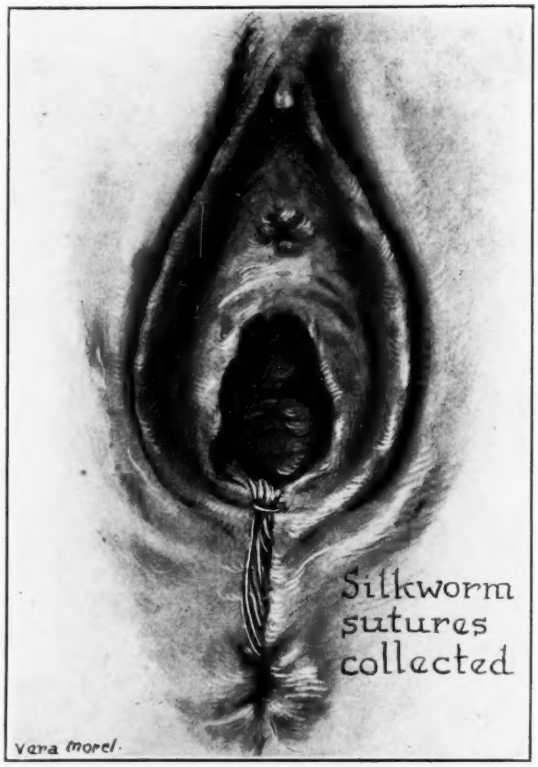

Fig. 5.—Final step shows the silkworm-gut sutures that have closed the perineal incision and extended to the forchette where they are gathered together and brought forward with one catgut suture to hold them together. This facilitates cleansing of the perineum postoperatively and prevents irritation during healing.

Postoperative Treatment.—The two principal aims are (1) to insure that there will be no bowel movement for at least seven days after operation, (2) to keep the operative field as mechanically clean as possible. Royston and other writers believe the optimum time for the first defecation to be between eleven and fifteen days after operation. In my opinion one week is usually adequate to obtain satisfactory results.

Beginning the first day after operation and continuing for six days, opium pills (1 gr. three times a day) are administered. In some cases

paregoric is substituted. The patient is kept on a nonresidue diet for as long as the opium is given; i.e., six days to one week and longer if it is found advisable. The nonresidue diet consists principally of water, tea, and coffee, and it does not include fruit juices which are prone to produce gas. In conjunction with the opium, this diet seems to appease the patient's appetite and causes no discomfort.

To maintain cleanliness, the patient is turned on her left side three or four times a day and the perineum is cleaned externally with a solution of potassium permanganate (1:10,000) or bichloride of mercury (1:10,000) or with a weak lysol solution, applied with cotton pledgets. The area is then dried and dusted with aristol powder or boric acid powder. Compresses of boric acid may be applied to the perineum to guard against infection. Royston thought it inadvisable to use pitcher or cleansing douches of any kind and that the wound should be left untouched. He stated that Plass proved twelve or thirteen years ago that untreated repairs heal best. Catheterization is often necessary, but it is better to have the patient void normally as fresh urine is seldom contaminating. Douches and enemas are absolutely not indicated until after the healing is completed nor should a rectal tube be used.

When it is desired to open the bowels on the seventh or eighth day, or later if circumstances so indicate, the patient should be given a cathartic, sometimes preceded by mineral oil. Castor oil is preferable to a saline purgative because the latter produces a liquid stool and does not soften the hard masses which are apt to form in the bowel after it has been kept constipated for seven days, and which are apt to put too much strain on the newly united ends of the sphincter muscles. In order to facilitate a defecation by softening the hard masses, we have found it advisable to instill two or three ounces of warm olive oil into the rectum with a small catheter when the patient feels the impulse to move the bowels. There is less tension if defecation occurs with the patient turned on her side.

The patient is placed on a soft diet when the bowels have acted well and a daily laxative or mineral oil is given, or when both are given so that the consistency is kept soft. If the area of repair is very extensive, the bowel movements should occur in the recumbent position for sixteen or eighteen days, and it is an additional measure of safety to continue the use of the bedpan even beyond this period. The patient should remain in bed for at least two weeks postoperatively.

A rise in temperature must be considered a danger signal of possible infection until it is proved to be otherwise. Compresses of hot boric acid or bichloride of mercury solution should be constantly kept applied to the perineum if infection is suspected. Should the catgut sutures break down, the silkworm-gut sutures, which are deeply placed, prevent separation of the suture line, and if infection can be controlled a successful outcome may still be expected.

Watchful care for ten or twelve days following operation is essential to the successful outcome of the operation. The importance of securing experienced nursing care cannot be overemphasized.

SUMMARY AND CONCLUSION

Review of 63 cases of complete tear of the perineum showed perfect control of anal sphincter in 49 cases, or 86 per cent; partial control in 7 cases and only 2 failures.

Success in obtaining perfect results is dependent upon preparation, upon the choice of operative procedure, and, to a very great extent, upon treatment after operation.

In order to provide complete restoration of the lost sphincter control, the operative procedure chosen should be the one best adapted to the extent of damage of the structures.

Treatment following operation should assure that there will be no bowel movement for at least seven days after operation, or until healing is effected; and that the perineal region be kept as nearly sterile as possible, at the same time avoiding the traumatizing effects of enemas, douches, and rectal tubes.

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AGGLUTININS IN THE SERUM AND BILE OF DOGS FOLLOWING CHOLECYSTITIS PRODUCED BY INJECTIONS OF TYPHOID BACILLI

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THERE is no specific etiologic factor known in cholelithiasis. Both cholecystitis and gallstones are known to be associated with infection. Typhoid fever, for example, has often been followed by cholelithiasis in the presence of a typhoid cholecystitis. In this paper the problem of infection and its relation to stone formation have been studied with respect to the immune bodies found in bile in the course of an experimentally induced typhoid cholecystitis.

Cushing,[1] who studied this subject in 1898, could not demonstrate antibody to be present in bile. However, in 1930, Freund and Henderson[2] showed that if immune serum was injected intravenously in rabbits the antibody could be found in bile. Although the intracholecystic agglutination of bacteria by specific antibody in bile might be a factor in stone formation, there are no reports in the literature indicating the correlation between the presence of infection in the gall bladder or elsewhere, the presence of antibody in bile, and the formation of gallstones. In the experiments reported in this paper the agglutinin titers of serum, gall-bladder bile, and hepatic bile were determined following the introduction of living typhoid bacilli into the gall-bladder wall. In a later paper we will report the data obtained in a clinical study of agglutinins in the gall-bladder bile of patients with biliary tract disease.

METHOD

Healthy, mongrel, female dogs were anesthetized with ether or sodium amytal. All operations were done under aseptic conditions. An upper right paramedian incision exposed the gall bladder and biliary ducts. The fundus of the gall bladder was isolated, with abdominal pads, and a portion of the gall-bladder bile was aspirated through a fine hypodermic needle (No. 22 gauge).

The subserous layer of the gall bladder was then infiltrated with 2 c.c. of an active twenty-four-hour culture of typhoid bacilli. This injection was done at a distance of 3 to 4 cm. from the original site of aspiration. Fine silk was used to ligate each puncture wound, and the abdomen was closed by tier suture.

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At the close of the observation period, which varied from six to twenty-eight days, another aseptic laparotomy was performed. The abdomen was opened through a right lateral rectus incision to avoid the previous scar. The gall bladder, biliary ducts, and duodenum were examined and the gall bladder was isolated by packing. The contents of the gall bladder were aspirated and the site of puncture was clamped. Cholecystectomy was then performed, following which the common duct was doubly intubated after the method of Rous and McMaster.[3] The abdomen was then closed by tier suture after providing stab wounds for the tubes leading from the proximal and distal portions of the common duct. Hepatic bile was collected under aseptic precautions during twenty-four-hour intervals. After several days the tubes were connected and the bile was allowed to flow into the small intestine.

Venous blood with obtained from each animal at the time of the experimental infection, at intervals during the experiment, and at its conclusion. The serum was used for estimation of circulating antibody.

A portion of each specimen of serum and bile was inoculated into beef infusion (pH 7.4) and the cultures and the centrifuged specimens of bile were examined by Gram's stain.

The agglutination tests were performed by serial arithmetic dilution of the serum and bile to a volume of 0.8 c.c. with isotonic buffered phosphate solution (pH 7.4) which contained 0.01 per cent thymol. Bacterial antigen was added so that the total volume was 1.0 c.c. The agglutination test tubes were incubated at 37° C. for twenty-four hours and were then examined with a hand lens for evidence of agglutination. Where there was any doubt about agglutination being present, the test tubes were centrifuged and the sediment was resuspended in 1.0 c.c. of physiologic saline solution and re-examined. Simultaneous controls in which the serum and bile of uninfected animals were tested against each of the antigens were included with each experiment. Parallel determinations of agglutination of *B. coli,* and *Staphylococcus aureus* by the test sera and bile specimens were included in order to provide a control for nonspecific agglutination. The original strains of bacteria were obtained through the courtesy of the Department of Bacteriology of the University of Pennsylvania. The typhoid bacillus (Strain 219T) was known to have a low virulence.

The organisms were kept in stock culture on agar slants and in beef infusion broth (pH 7.4). Stock cultures were transferred every five to six weeks. Antigen was prepared from 250 c.c. of beef infusion broth in which the organisms had been cultivated for twenty-four hours at 37° C. After centrifuging, the supernatant clear fluid was decanted and the bacterial residue was washed twice with physiologic salt solution and was then resuspended in 25 per cent of the original volume with normal saline solution. The organisms were killed with

thymol (0.1 per cent), and after twenty-four hours in the refrigerator the bacterial antigen was tested for sterility.

The antigens were diluted to contain four to five million organisms per cubic centimeter. These antigens were discarded when spontaneous agglutination or contamination occurred. No antigen was used for more than fifteen days. Gram stains were performed daily on all antigens and cultures in use.

When the gall bladder was removed, it was opened and examined immediately. After fixation in formalin, histologic sections stained with hematoxylin-eosin and methylene blue were prepared.

RESULTS

Typhoid cholecystitis was produced in 16 dogs in which the biliary tract appeared normal before the experimental infection. The animals showed very slight constitutional reaction to the infection and none of the animals died.

The gall-bladder bile was sterile prior to the induced infection. Blood cultures were sterile. The gall-bladder bile at the time of the second operation contained the typhoid bacillus in 12 of 14 animals (85 per cent) in which the bile was available for culture. The typhoid bacillus was found in the hepatic bile in 6 of 7 animals within eighteen days of the experimental infection, and in only 1 of 9 animals after eighteen days.

The gall bladders which were removed six to fourteen days after the infection presented the gross and microscopic picture of an acute inflammation, the most prominent features being mural edema and cellular exudation. The incidence of bacteria in the gall-bladder wall as seen in histologic section was highest in this stage. From fifteen to twenty-two days after the infection the gross and microscopic picture was that of a subsiding infection. Hyperplasia was present and there was an excess of lipoid in the epithelial cells. After twenty-two days the gall bladder showed a chronic cholecystitis with early to advanced fibrosis. The excised gall bladder always presented a gross and microscopic picture of acute or chronic infection varying in its histologic pattern in relation to the interval from the induced experimental infection to the time of cholecystectomy.

Table I shows the agglutinin values of the serum, gall-bladder, and hepatic biles obtained at different periods following experimental infection. Three animals (Nos. 21, 23, and 852) showed significant agglutinin levels in serum and gall-bladder bile even before infection. These are included in Table I in order that the relative significance of spontaneous immunity in the group may be assessed. Two of these were subjected to cholecystectomy six days after infection, and both showed a marked rise in titer of serum, with little change in the level of agglutinin in the bile. The mean values shown at the bottom of

TABLE I

DOG	BILE	DAY							
		1	4	6-7	8-10	12-14	15-18	19-22	23-28
21	Serum	200		800					
	Gall-bladder	80		40					
	Hepatic			20					
24	Serum	100		1600					
	Gall-bladder	80		160					
	Hepatic	0		80					
867	Serum	0		80		1000			
	Gall-bladder	0							
	Hepatic					20			
524	Serum	10		160		2000			
	Gall-bladder	0							
	Hepatic					80			
18	Serum		500		3200				
	Gall-bladder	0					80		
	Hepatic								
852	Serum	1600		3200			2000		
	Gall-bladder	480					320		
	Hepatic						80		
295	Serum	0				160	320		
	Gall-bladder	0					40		
	Hepatic								
296	Serum	50			320		{640		
							{640		
	Gall-bladder	5					40		
	Hepatic						10		
297	Serum	50					{320		
							{640		
	Gall-bladder	0					20		
	Hepatic						10		
308	Serum	0				160	320		
	Gall-bladder	0					–		
	Hepatic						10		
320	Serum	6			320		640	640	
	Gall-bladder	0						320	
	Hepatic							80	
319	Serum	6			320		320	160	
	Gall-bladder	2.5						40	
	Hepatic							10	
269	Serum	40	320				640	80	
	Gall-bladder	0						20	
	Hepatic							2.5	
298	Serum	6			320		640		160
	Gall-bladder	0							80
	Hepatic								10
31	Serum	20			320		1250		{160
									{160
	Gall-bladder	0							40
	Hepatic								{ 5
									{ 20
34	Serum	40			{2000				{320
					{ 640				{320
	Gall-bladder								80
	Hepatic								{ 10
									{ 10
Average, excluding No. 852	Serum	37.7	410	670	930	830	579	300	224
	Gall-bladder	11.2		100			45	123	66.6
	Hepatic			50		50	10.0	31	11

the table, while having no accurate mathematical significance, will indicate the trend of the agglutinin values obtained. One animal (No. 852) is excluded in this average in order to afford greater statistical accuracy. The serum agglutinin reached a peak between the seventh and tenth days, and by the twenty-eighth day had returned almost to the control level. The gall-bladder bile agglutinin tended to lag behind the serum titer and did not reach a peak until the end of the third week. The curve of agglutinin in hepatic bile followed rather closely the serum curve.

The parallel determinations of agglutination of *B. coli* and *Staphylococcus aureus* failed to show any significant fluctuations during the period of observation. There were minor and transient alterations in the agglutinating power of serum and bile against these organisms, but the contrast between these alterations and those obtained from *B. typhosus* was sufficiently great to establish the specificity of the antibody reaction in this type of infection.

In two instances small calculi were found attached to the gall-bladder wall. These calculi were hard, brittle, greenish black, and from 2 to 3 mm. in diameter. These were found in one dog eighteen days and in the other twenty-two days after the induced cholecystitis. Microscopic examination showed that many clumped bacilli resembling the typhoid bacillus were present in the calculi.

The gall-bladder bile of two other dogs contained foreign substances. In one animal the material was in the form of mucoid pellets which were translucent, grayish green, and about 3 mm. in diameter. In the other instance the bile contained a coarsely granular dark pigmented sediment.

DISCUSSION

Bacterial cholecystitis has been found to be due to an intramural and submucosal infection.[4-7] However, the importance of other factors in the production of cholecystitis and cholelithiasis, such as trauma and stasis, has been stressed. The significance of the factor of trauma which entered into the experiments here reported is difficult to evaluate.

The gall-bladder bile was sterile prior to the experimental infection. Cultures taken at the time of cholecystectomy were positive for the typhoid bacillus in 85 per cent of the animals. The gall bladders of all of the animals showed microscopic evidence of infection, including those with sterile bile. Clinically, it has been demonstrated that from 42 to 65 per cent of individuals who have cholecystitis have bacteria present in their bile.[9, 10] The absence of a positive culture does not necessarily rule out an infectious origin of the cholecystitis, the presence of the organisms being simply confirmatory evidence.

Culture of the hepatic bile revealed the typhoid bacillus to be present in every sample collected prior to eighteen days following the

experimental infection. After eighteen days the typhoid bacillus was found in only one instance (at twenty-six days). These results indicate that an associated cholangitis was present, a lesion which often accompanies cholecystitis.[11]

Upon microscopic examination of the excised gall bladders, the common findings were edema, fibrosis, and cellular infiltration of the wall, the degree of alteration from normal depending upon the interval which had been allowed to elapse since the initiation of the experimental infection. Significant changes were also present in the epithelium, including hyperplasia, hypertrophy, and an increase in the lipoid content of the epithelial cells. These observations agree with those reported in the literature where both mural[9] and epithelial[12] changes have been shown to exist in various phases of cholecystitis.

The rise in the agglutinin titer in the serum in response to induced typhoid cholecystitis agrees with reports in the literature. The response in the serum to any antigen or infection is usually a typical one, but may be modified by a number of factors.[13-18]

It might be expected that the agglutinin which appears in serum will also appear in bile, just as it appears in other body fluids. Passive immunization with antiserum[2] as well as active immunization with vaccine[19] will augment the antibody content of both serum and bile. In these experiments a specific agglutinin was found in the serum after an experimental infection, and the same antibody was found in the hepatic bile and in the gall-bladder bile.

The typhoid agglutinin in the serum was always greater than the similar agglutinin in the hepatic bile. The agglutinin in the gall-bladder bile was always greater than the similar agglutinin in the hepatic bile. The experimental evidence available, however, does not show that a definite ratio exists. The relation of hepatic bile, gall-bladder bile, and serum agglutinin varied with agglutinin, with the animal, and with the mode of production of the antibody.[2, 19] It seems probable that the high levels of gall-bladder bile agglutinin found at about twenty-one days, in spite of reduced serum values, were due to improvement in the concentrating power of the gall bladder with subsidence of the acute infection.

Calcification present in the epithelium,[22] calculus-like pigmented sediment,[5] and mucous pellets[20] as observed in this experiment have also been reported with clinical and experimental infection. Since typhoid bacilli have been found within gallstones,[1, 21] it is of interest to have found bacilli present in the mural calcifications formed in these dogs after an induced infection and in the presence of bacterial agglutinin.

SUMMARY

1. Suspensions of an avirulent strain of typhoid bacillus were injected into the gall bladders of healthy dogs.

2. The typhoid bacillus was identified in the gall-bladder bile (85 per cent) at intervals of from six to twenty-seven days after the induced cholecystitis.

3. Cholangitis accompanied the induced infection until eighteen days after the onset.

4. Histopathologic examination of the gall bladder showed a varying picture. The usual findings of infection were present and mural edema and fibrosis accompanied normal or altered epithelium in which there was often an increase in lipoid content.

5. Coal dust pigmented detritus and mucous pellets were found in the gall-bladder bile.

6. Small stones were found in two instances in which clumped bacilli were present.

7. The induced cholecystitis produced the appearance of a specific agglutinin in the serum, in the gall-bladder bile, and in the hepatic bile.

8. The gall bladder concentrates the agglutinin in the hepatic bile, and the concentrating power of the gall bladder increases as the gall bladder recovers from infection.

In conclusion, the onset of a bacterial cholecystitis stimulated the appearance of a specific agglutinin in the serum, in the gall-bladder bile, and in the hepatic bile. In two instances stones were found to be present in the gall bladder.

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INTESTINAL OBSTRUCTION CAUSED BY GALLSTONES

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THE rarest of all the reasonable ways in which the intestine may become obstructed is by gallstones. Gallstones, however, frequently reach the alimentary tract through the common bile duct and occasionally through a fistula between the gall bladder or bile passages and the intestines or stomach. In cases in which intestinal obstruction has been produced by gallstones, the stone or stones usually have passed through fistulas.

The estimation of the frequency of the occurrence of gallstone ileus is now practically impossible. Wagner found that 334 cases had been recorded in the literature prior to 1914. In 1925 Moore estimated that 400 cases had been recorded. At the Mayo Clinic we have observed 10 cases in which intestinal obstruction was proved to be the result of gallstones. In these cases the obstruction was produced in one of three ways: (1) The stone was too large to pass through the lumen of the intestine; (2) the stone produced intussusception; or (3) the stone became embedded in the wall of the intestine and closed its lumen. In all of these cases it is probable that the stone or stones were too large to pass through the lumen of the intestine and that the intussusception or the inflammatory mass was a secondary reaction.

Table I shows the clinical findings in the 10 cases. Eight of the 10 patients were women and 2 were men. Only 3 of the patients had had definite symptoms of chronic cholecystic disease. Two had had indefinite symptoms. The rest of the patients had not had symptoms which are ordinarily associated with chronic cholecystic disease.

Cases in which intestinal obstruction is the result of gallstones may be divided into two groups, depending on whether or not there have been symptoms of chronic cholecystic disease: (1) those in which the patients have had recurring attacks of intestinal obstruction prior to the onset of complete ileus, and (2) those in which the patients have apparently been in good health prior to the onset of ileus. Of the 10 cases in this series, 5 belonged to the first group and 5 belonged to the second group. In all of the cases the gallstones had passed through a perforation in the gall bladder. In some cases the cystic and common bile ducts possibly may dilate sufficiently to allow the passage of a stone that is large enough to produce an ileus, but we have not

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TABLE I

CLINICAL FINDINGS IN CASES OF INTESTINAL OBSTRUCTION BY GALLSTONES

CASE	AGE, YEARS, SEX	SYMPTOMS CHARACTERISTIC OF CHOLECYSTIC DISEASE	SYMPTOMS OF INTESTINAL OBSTRUCTION	SITUATION OF FISTULA BETWEEN BILE PASSAGES AND ALIMENTARY CANAL	SITUATION OF INTESTINAL OBSTRUCTION	STONES PRESENT IN BILE PASSAGES	DIAGNOSIS MADE AT
1	31 F	None	Definite	Gall bladder to duodenum and suprarenal gland	Duodenum	No	Necropsy
2	44 F	Indefinite	Recurring	Gall bladder to duodenum and pancreas	Duodenum	No	Operation
3	44 M	Definite	Recurring	Gall bladder to hepatic flexure of colon	Colon	Yes	Operation
4	49 M	None	Definite	Gall bladder to duodenum	Duodenum	No	Operation
5	58 F	None	Definite	Gall bladder to duodenum	Distal portion of ileum	No	Operation
6	64 F	Definite	Recurring	Gall bladder to duodenum	Indefinite; progressed distally	Yes	Operation
7	65 F	Indefinite	Recurring	Gall bladder to duodenum	Indefinite; progressed distally	Yes	Operation
8	70 F	Definite	Recurring	Gall bladder to duodenum	Small intestine	Yes	Operation*
9	74 F	None	Definite	Gall bladder to duodenum	Distal portion of ileum	Yes	Necropsy
10	76 F	None	Definite	Gall bladder to duodenum	Distal portion of ileum	Yes	Necropsy

*Died after operation.

observed such a case. It is our opinion that a gallstone that is large enough to cause intestinal obstruction usually reaches the intestine in only one way; that is, through a cholecystoenteric fistula. The fistula may not remain patent. At the time of operation or necropsy, the only evidence of a fistula frequently is the presence of adhesions.

Two of the 4 cases in which the obstruction was situated in the terminal portion of the ileum are of interest. In each of these cases the stone had passed distally for some distance but finally had to be removed. During the passage of the stones distally, the intensity of the symptoms of intestinal obstruction had slowly decreased.

If perforation of the gall bladder would permit the discharge of all the stones into the intestine, such an occurrence might not be a great catastrophe. However, perforation of the gall bladder and the subsequent formation of a cholecystoenteric fistula do not always empty the gall bladder and bile ducts of stones. In 6 of the 10 cases stones were still present in the gall bladder or bile passages when the patients were operated on or came to necropsy.

Intestinal obstruction by gallstones, as has been stated, in our experience has usually been secondary to the formation of a cholecystoenteric fistula which has resulted from the perforation of an inflamed gall bladder into the intestine. In no case had a peptic ulcer or carcinoma perforated into the gall bladder and allowed the stones to pass through the perforation and obstruct the intestine. A study of 176 cases of cholecystoenteric fistula disclosed that the perforation involved the following structures: the gall bladder and duodenum in 101 cases, the gall bladder and colon in 33 cases and the gall bladder and stomach in 7 cases. In 24 there were multiple perforations and stones were discharged into the abdominal cavity or into adjacent structures, and in 11 there were multiple perforations between the gall bladder, adjacent organs, and alimentary canal. From the foregoing data one can surmise that the site of intestinal obstruction by gallstones is usually in the small intestines. The clinical data in Table I show that in 1 of our cases the obstruction involved the small intestine.

Intestinal obstruction secondary to a chronic cholecystic disease followed by a perforation of the gall bladder may occur without the gallstones actually passing into the lumen of the intestine. In 2 cases (data not included in the table) the gall bladder had perforated onto the mesentery of the small intestine and the subsequent tumefaction and abscess formation were sufficient to produce the clinical signs and symptoms of intestinal obstruction. After appropriate surgical treatment, both of the patients recovered.

In cases in which intestinal obstruction is caused by gallstones, the cause of the obstruction rarely is suspected before operation or necropsy is performed. In the 10 cases in this series the diagnosis of the cause of the obstruction was made at operation or necropsy. There is nothing characteristic about intestinal obstruction that is caused by gallstones. In practically all cases of intestinal obstruction, the condition is preceded by minor and repeated symptoms that are indicative of varying degrees of obstruction. A history of chronic cholecystic disease is of no value. In many cases of intestinal obstruction, regardless of the cause, the patients have or have had chronic cholecystic disease.

COMMENT

Since the brilliant treatise on the clinical diagnosis and surgery of the gall bladder and bile passages by Courvoisier in 1890, many of the usual and unusual clinical observations concerning perforation and obstruction of the gall bladder and bile passages and intestines by gallstones have been recorded. Intestinal obstruction by a gallstone or gallstones has been reason enough to record the case history of such an illness. The recording of unusual case histories is commendable, provided physicians and surgeons do not lose perspective and try to

estimate the frequency of such an unusual occurrence by the number of case histories to be obtained from a review of the literature.

When the intestine is obstructed by a gallstone, the obstruction usually is situated in the distal portion of the ileum. However, the obstruction may be situated at any narrowed portion of the alimentary tube.

For a correct diagnosis the clinician must depend on the surgeon or the post-mortem findings. The treatment, as in other cases of intestinal obstruction, is surgical except under very extraordinary circumstances.

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CHOLECYSTOENTERIC FISTULAS

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IN CASES in which gallstones are associated with repeated colics, it is reasonable to assume that the stones are often discharged through the bile passages into the intestine. If the stone can pass through the bile ducts and reach the intestine, no serious complication arises. It has been stated that stones thus discharged have caused intestinal obstruction. However, at the Mayo Clinic we have not observed a case in which intestinal obstruction resulted from stones thus discharged. The passage of gallstones through cholecystoenteric fistulas is not a common occurrence. It is the object of this paper to record 176 cases of cholecystoenteric fistula.

A cholecystoenteric fistula may be produced in one of three ways: (1) by perforation of the gall bladder and intestine by gallstones, (2) by perforation of the intestine and gall bladder by a peptic ulcer, and (3) by perforation of the intestine and gall bladder by a carcinoma. In none of the 176 cases recorded was the obstruction the result of a perforated ulcer or carcinoma. Therefore, we limit this report to fistulas which arose primarily from biliary disease.

In the 176 cases the situation of the fistula was as follows: between the gall bladder and duodenum in 101 cases, between the gall bladder and the colon in 33 cases, and between the gall bladder and the stomach in 7 cases. Multiple fistulas between the gall bladder and adjacent organs and alimentary tube were found in 11 cases. In 24 cases the gall bladder had ruptured and the stones had been discharged into the abdominal cavity.

The age of the 101 patients who had fistulas between the gall bladder and the duodenum varied; 3 of the patients were less than 40 years of age and 25 were between 40 and 49 years of age. The highest incidence was between the ages of 60 and 69 years. Only 8 patients were past 70 years of age. Seventy-one of the patients were women and 30 were men.

The ages of the 32 patients who had cholecystocolic fistulas were as follows: One patient was less than 30 years of age; 2 were between 30 and 37 years of age; 8 were between 40 and 49 years; 9 were between 50 and 59 years; 10 were between 60 and 69 years; and 2 were

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more than 70 years of age. Of this group of patients, 19 were men and 13 were women.

The ages of the 24 patients whose gall bladders had ruptured into the abdominal cavity varied as follows: One was less than 30 years of age; 1 was between 30 and 39 years; 2 were between 40 and 49 years; 10 were between 50 and 59 years; 8 were between 60 and 69 years; and 2 patients were in the eighth and ninth decades of life respectively. Fifteen of the patients were men and 9 were women.

The ages of the 7 patients who had fistulas between the gall bladder and stomach and the 11 who had multiple cholecystoenteric fistulas varied from 20 to 80 years. Two were less than 30 years of age; 2 were between 30 and 39 years; 5 were between 40 and 49 years; 3 were between 50 and 59 years; 4 were between 60 and 69 years; 1 was between 70 and 79 years; and 1 had passed his eightieth year. Of the 18 patients, 10 were women and 8 were men.

It is usually stated that in cases of chronic cholecystic disease the ratio of women to men is about 2:1. However, in this series of cases there were 103 women and 73 men. We believe that the increased number of women who have cholecystic fistulas can be accounted for by the usual preponderance of chronic cholecystic disease among women. There was nothing unusual in the age distribution in any of the groups or in the total number of cases. The greatest incidence of cholecystic fistulas was in the seventh decade of life.

The clinical history of the patients who had cholecystoduodenal fistulas was no different than the history obtained in cases of ordinary uncomplicated chronic cholecystic disease.

In 11 of the cases of cholecystoduodenal fistula the clinical histories were not definite. There had been periods during which the symptoms had been rather typical of chronic cholecystic disease which had subsided. Following these periods the illness had been characterized by chills and a low grade fever. There had not been very much abdominal distress. The symptoms of the 11 patients, however, were no different from the symptoms in the cases in which a subacute cholangitis developed during the course of chronic cholecystic disease.

Owing to the close proximity of the gall bladder and the colon, the colon is frequently perforated by a diseased gall bladder. When there is a cholecystocolic fistula the symptoms of chronic cholecystic disease without a marked degree of cholangitis are changed to symptoms of definite cholangitis. Of the 32 patients who had cholecystocolic fistulas, 19 recently had lost from fifteen to forty pounds. Two also had had severe chills, high fever, and protracted diarrhea. In the rest of the cases the chills and fever had not been accompanied by diarrhea. Seven of the 32 patients who had cholecystocolic fistulas were not seriously ill.

When the gall bladder becomes acutely inflamed and contains stones, it may perforate into the abdominal cavity. This occurred in 24 of the cases in this series. In such cases the patients usually give a history of chronic cholecystic disease. The perforation of the gall bladder into the abdominal cavity may be a very serious complication of chronic cholecystic disease. However, the perforation often occurs slowly and the abscess cavity containing the stones is completely walled off by the omentum and the complication is masked by the clinical syndrome of acute cholecystitis and probably cholangitis. In only 5 of the 24 cases had the gall bladder perforated and stones been discharged directly into the abdominal cavity. In 3 of the 24 cases the gall bladder had perforated into the mesentery. The mesenteric abscess thus produced had caused symptoms of intestinal obstruction.

Cholecystogastric fistulas usually do not produce any untoward symptoms. This fact is well known as a result of the frequency with which relief has been obtained by a surgical anastomosis of the gall bladder to the stomach in cases in which carcinoma is situated at the head of the pancreas.

It is important to remember that fistulas between the gall bladder and the alimentary tube or adjacent organs may not always occur singly. In 11 of the cases in this series there were multiple fistulas. In the 11 cases the fistulas were usually situated between the gall bladder and the duodenum and liver. A perforation of the gall bladder into the alimentary tube is apparently of less serious importance than is the perforation and discharge of the stones into the parenchyma of the liver or into adjacent structures. In the first place a communication between the gall bladder and intestine permits discharge of at least some of the gallstones into the intestines and permits some drainage. In the second place, when the gall bladder perforates into an adjacent organ, the formation of an abscess is inevitable.

COMMENT

The bizarre and unusual instances of perforation of the gall bladder and migration of gallstones may be recalled by stating that gallstones have been seen in the pelvis of the kidney, in a persistent urachus, in the urinary bladder, in ovarian cysts, in a pregnant uterus, in the precordial cavity, and in the bronchial tubes. Fortunately, however, most gallstones that are spontaneously discharged from the body are either vomited or passed in the feces. The presence of gallstones in vomitus or feces does not always indicate the presence of a fistula.

The diagnosis of a cholecystoenteric fistula usually cannot be made by the clinical history or physical examination. Occasionally, the fistula can be demonstrated by roentgenologic examination. The presence of a fistula does not necessarily mean that all the gallstones have

been discharged into the intestine. Patients who have had a cholecystoenteric fistula have been known to enjoy good health for a long time. However, patients who have chronic cholecystic disease frequently enjoy a comparative freedom of symptoms for a long time. In either case it is not safe to "observe" the patients, because a cholangitis and hepatitis frequently will develop, or the bile duct or the fistula will become obstructed, and the subsequent jaundice will turn a relatively safe surgical procedure into one that is difficult for the surgeon and particularly dangerous for the patient.

LUDWIG'S ANGINA

An Anatomical and Clinical Study With Review of the Literature

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THE term Ludwig's angina has been of rather vague significance in the minds of most surgeons since the first definite description by Ludwig (1836). A variety of conditions have been described as Ludwig's angina until the term has largely lost its significance as a clinical entity. In fact, as early as 1892 there was serious debate as to whether its consideration as a clinical entity was justified or not. One of the most active champions for retention of the name and its recognition as an entity was Delorme (1892), while on the other side, equally as active, was Nelatón (1892).

There are records of neck infections preceding Ludwig's classic description, but most of these are vague and inconclusive. Fothergill's description of "putrid sore throat" (1769) resembles Ludwig's angina only slightly. Gregory (1822), on the other hand, described a case which was undoubtedly one of Ludwig's angina and quoted similar cases by James of Exeter, Kirkland, and Willis.

Ludwig himself (1836), after giving his case history, emphasized the following points: (1) the comparative slight inflammation of the throat itself; (2) the peculiar "woody" hardness of the cellular tissue, on which an impression cannot be made; (3) the hard swelling under the tongue and the swelling of the floor of the mouth on the inner border of the mandible; (4) the well-defined border of hard edema in the neck; and (5) the absence of infection in the regional lymph nodes.

This description has been quoted by several later investigators and yet some of them insisted that the primary spread from the floor of the mouth to the submaxillary fossa was by lymphatics, and the later spread, back to the floor of the mouth and inferiorly in the neck, by fascial planes (Thomas, 1908; Muckeston, 1928). This view probably was based on the observation that the first demonstrable swelling is often in the submaxillary triangle of one or both sides with later swelling of the floor of the mouth. However, the external evidence of swelling is hardly proof of the portal of entry or means of transmission. Furthermore, some cases show their first visible swelling in the floor of the mouth and, according to the findings of most investigators, including Ludwig, the lymph nodes are not involved in the process.

Davis (1906), Blassingame (1928), Ashhurst (1929), Dehart (1933), Berryhill (1933), and others insisted that the spread was from the floor

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of the mouth to the submaxillary region of one or both sides by tissue planes and not by lymphatics. This view would seem to fit Ludwig's original description as well as the anatomic and clinical findings of later investigators.

If the term Ludwig's angina is to be retained, as it no doubt will, it should be used to refer to a specific clinical entity and not to a variety of conditions, similar only in minor points or in their end results. From a study of the literature in which I have reviewed eighty-six articles from 1769 to 1938, including the original article by Ludwig (1836), I feel that the term Ludwig's angina should be reserved to refer to those cases of infection starting in the floor of the mouth, usually from carious lower molar or bicuspid teeth, spreading to the submental and submaxillary triangles (submandibular space) by fascial planes, and causing serious symptoms from edema of the tongue and glottis, mediastinitis, or toxemia. This definition automatically rules out spread by lymphatics, though obviously a periadenitis may lead to secondary fascial plane infection. It also practically eliminates the throat, tonsils, and pharynx as the seat of the initial lesion. Infections in these structures spread by lymphatics, or form retropharyngeal or lateral pharyngeal abscesses, which in turn spread secondarily to the submandibular space and resemble Ludwig's angina in the later stages.

ANATOMY

In order to fully appreciate the pathologic anatomy of Ludwig's angina, one must be familiar with the normal anatomy of the head and neck. In a previous article, Holyoke and I (1938) have reviewed the literature and given our description of the fasciae and fascial spaces of the head, neck, and adjacent regions based on the study of 75 adult cadavers and 5 full-term fetuses by dissection, injection, and section methods. It may be desirable to review this description at this time.

Layers of Fascia.—The superficial fascia is a continuous sheet of fatty tissue extending from the head and neck into the regions of the thorax, shoulders, and axillae. In the neck it is a moderately loose layer containing the platysma muscle in its deep portion. In the face the superficial fascia is very adherent to the overlying skin and contains the muscles of expression in its deep portion.

Superficial Layer of Deep Fascia: This layer crosses the anterior triangle of the neck, splits to form the sheath of the sternocleidomastoid muscle, crosses the posterior triangle, splits to form the sheath of the trapezius muscle and finally attaches to the spines of the vertebrae in the midline posteriorly. In the midline anteriorly it splits to form the suprasternal space of Burns, its anterior and posterior leaflets attaching to the corresponding margins of the sternum. Lateral to the sternum, it is attached inferiorly to the clavicle, acromium, and spine of the scapula. A corresponding layer, the superficial layer of deep pectoral

fascia, then continues from the anterior inferior surface of the clavicle around the pectoralis major muscle and at the lateral inferior border of this muscle becomes the deep axillary fascia, which crosses the axilla and splits to form the sheath of the latissimus dorsi muscle. (Figs. 1, 2, 6, 7.)

Superiorly the superficial layer of deep fascia attaches to the hyoid bone and proceeds across the submental and submaxillary triangles (submandibular space). It fuses with the sheath of the anterior belly of the

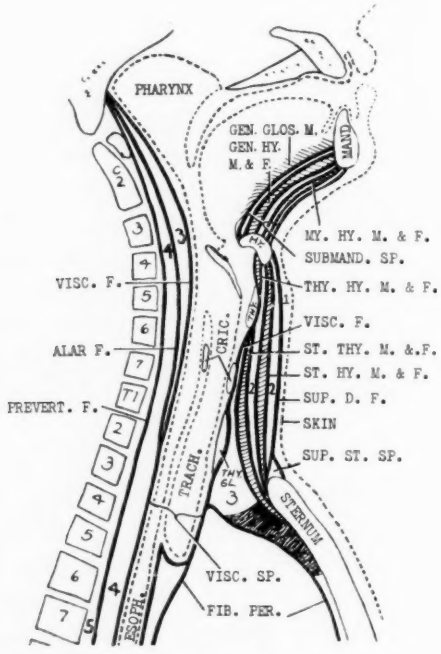

Fig. 1.—Diagrammatic drawing of fasciae of head and neck in midsagittal section.

Key to Illustrations

ALAR F., alar fascia; *AX. SP.*, axillary space; *ARYT.* arytenoid cartilage; *A. AOR.*, ascending aorta; *BR. PL.*, brachial plexus; *CLAV.*, clavicle; *CORAC.*, coracoid process; *CRIC.*, cricoid cartilage; *C.C.A.*, common carotid artery; *CONST. PHAR. SUP. M.*, superior pharyngeal constrictor muscle; *D. D. PECT. F.*, deep layer of deep pectoral fascia; *DELT. M.*, deltoid muscle; *DIG. ANT. M.*, digastric muscle, anterior belly; *DIG. POST. M.*, digastric muscle, posterior belly; *E.C.A.*, external carotid artery; *E. MAX. A.*, external maxillary artery; *EPIGL.*, epiglottis; *ESOPH.*, esophagus; *EUST. TUBE*, Eustachian tube; *GEN. GLOS. M.*, genioglossus muscle; *GEN. HY. M.*, geniohyoid muscle; *GLOT.*, glottis; *HY.*, hyoid bone; *HY. GLOS. M.*, hyoglossus muscle; *I.C.A.*, internal carotid artery; *I.J.V.*, internal jugular vein; *LEV. VEL. PAL. M.*, levator veli palatini muscle; *LAT. PHARYNG. SP.*, lateral pharyngeal space; *L.A.*, lingual artery; *L.N.*, lingual nerve; *MAND.*, mandible; *MASTIC. SP.*, masticator space; *MAST. PROC.*, mastoid process; *MAX. S.*, maxillary sinus; *MY. HY. M.*, mylohyoid muscle; *OCCIP. BONE*, occipital bone; *OM. HY. M.*, omohyoid muscle; *PAROT. GL.*, parotid gland; *PECT. MAJ. M.*, pectoralis major muscle; *P.F.V.*, posterior facial vein; *PREVET. F.*, prevertebral fascia; *PT. INT. M.*, internal pterygoid muscle; *PT. EXT. M.*, external pterygoid muscle; *PHR. N.*, phrenic nerve; *SCAL. F.*, scalenus fascia; *SCAL. ANT. M.*, scalenus anterior muscle; *SCAL. MED. M.*, scalenus medius muscle; *SCAL. POST. M.*, scalenus posterior muscle; *ST.*, sternum; *SCAP.*, scapula; *SUP. D.F.*, superficial layer of deep fascia; *SUP. D. PECT. F.*, superficial layer of deep pectoral fascia; *SUBMAND. SP.*, submandibular space; *SUP. ST. SP.*, suprasternal space; *SUBMAX. GL.*, submaxillary gland; *ST. CL. M.*, sternocleidomastoid muscle; *ST. HY. M.*, sternohyoid muscle; *ST. THY. M.*, sternothyroid muscle; *STY. HY. M.*, stylohyoid muscle; *STY. GLOS. M.*, styloglossus muscle; *STY. PHAR. M.*, stylopharyngeus muscle; *SUBCLAV. M.*, subclavius muscle; *SYM.*, sympathetic trunk; *TEMP. M.*, temporalis muscle; *THY.*, thyroid cartilage; *THY. GL.*, thyroid gland; *TRACH.*, trachea; *TEN. VEL. PAL. M.*, tensor veli palatini muscle; *TRAP. M.*, trapezius muscle; *THY. HY. M.*, thyrohyoid muscle; *VISC. F.*, visceral fascia; *VISC. SP.*, visceral space; *V.N.*, vagus nerve; *ZYG.*, zygoma.

digastric muscle, although the two layers may be easily separated. It also becomes attached to the sheaths of the stylohyoid and posterior belly of the digastric muscles, and then splits to form the capsule of the submaxillary salivary gland. This is a completely closed capsule which attaches superiorly by two slips to the superficial and deep margins of the body of the mandible. The anterior belly of the digastric, the mylohyoid, the geniohyoid, the genioglossus, and the hyglossus have independent sheaths with bony attachments at the attachments of these muscles. (Figs. 1, 3, 5, 8.)

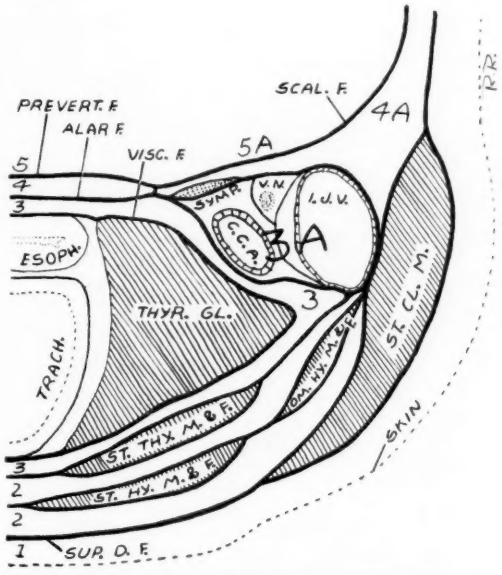

Fig. 2.—Diagrammatic drawing of fasciae of neck. Transverse section approximately at the level of the sixth cervical vertebra.

Between the angle of the jaw and the anterior border of the sternocleidomastoid muscle, the superficial layer of deep fascia splits to form the capsule of the parotid gland which in our experience is complete on all sides. From the body of the mandible, the superficial layer of deep fascia extends superiorly to form the sheath of the masseter muscle and attaches to the zygoma above. It then continues superiorly over the temporal muscle as the outer layer of deep temporal fascia. At the anterior and posterior borders of the masseter, it passes around the corresponding borders of the ramus of the mandible and becomes continuous with the sheaths of the pterygoid muscles, thus completing the walls of the masticator space (see below). (Figs. 3, 4, 8.)

Middle Layer of Deep Fascia: This consists of three subdivisions, the sternohyoid-omohyoid layer, the sternothyroid-thyrohyoid layer, and the visceral layer. The former is continuous across the midline anteriorly, forms the sheaths of the sternohyoid and omohyoid muscles, and attaches to the deep surface of the sternocleidomastoid sheath, where it forms a

pulley between the anterior and posterior bellies of the omohyoid muscle. Superiorly it is attached to the hyoid bone and, more laterally, to the overlying superficial layer of deep fascia and underlying sternothyroid-thyrohyoid layer along the superolateral border of the anterior belly of the omohyoid muscle. Likewise, in the posterior triangle, it is attached along the superolateral border of the posterior belly of the omohyoid muscle to the superficial layer of deep fascia. Inferiorly this layer is attached to the sternum, clavicle, and scapula. A corresponding layer, the deep layer of deep pectoral fascia, starts at the clavicle, splits to form the sheath of the subclavius muscle, becomes the costocoracoid membrane, splits to form the sheath of the pectoralis minor muscle, and becomes the suspensory ligament of the axilla which runs into the axillary fascia. (Figs. 1, 2, 6-8.)

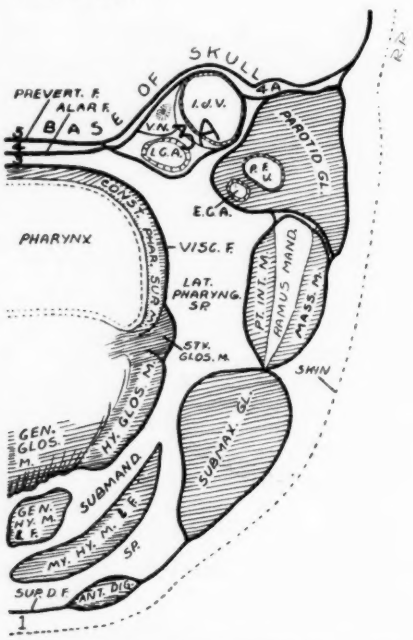

Fig. 3.—Diagrammatic drawing of fasciae of the head and neck. Oblique anteroposterior section showing the relation of the submandibular space to the lateral pharyngeal space and Spaces 3 and 4.

The sternothyroid-thyrohyoid layer crosses the midline anteriorly, splits to form the sheaths of the muscles indicated in the name, and laterally runs into the deep surface of the sternocleidomastoid sheath, fusing here with the carotid sheath. Inferiorly it attaches to the sternum and clavicle. Superiorly it attaches to the thyroid cartilage and hyoid bone; more laterally to the superficial layer of deep fascia and the sternohyoid-omohyoid layer superficially, and the carotid sheath deeply. (Figs. 1, 2, 6-8.)

The visceral fascia completely surrounds the thyroid gland, trachea, and esophagus. Superiorly, it extends to the base of the skull on the posterior side, and to the thyroid cartilage and hyoid bone on the ante-

rior and lateral sides. Inferiorly at the root of the neck it fuses with the alar fascia of the anterior wall of the carotid sheath and becomes continuous with the fibrous pericardium covering the heart and great vessels of the thorax. It also continues inferiorly as the covering of the thoracic portion of the trachea and esophagus. (Figs. 1-8.)

Deep Layer of Deep Fascia: There are two main subdivisions, the alar and prevertebral fasciae, including the continuations of the latter; eg., scalenus, transversalis, and Sibson's fasciae.

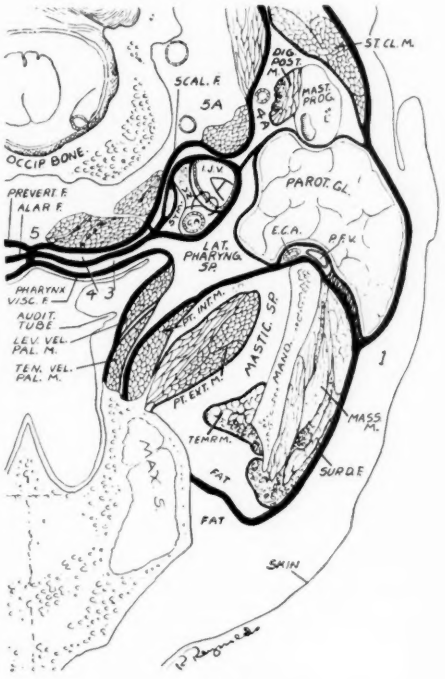

Fig. 4.

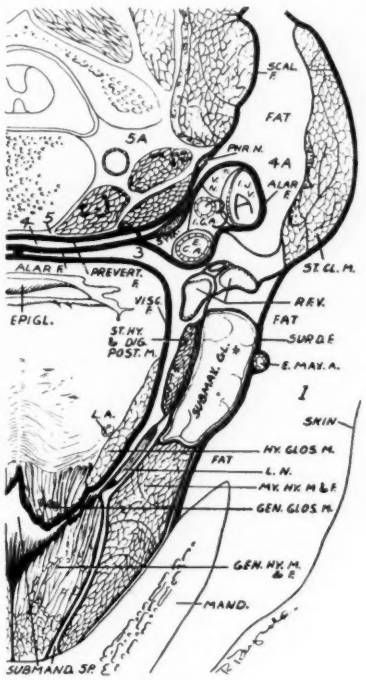

Fig. 5.

Fig. 4.—Transverse section of adult cadaver at level of hard palate. Superior view.
Fig. 5.—Transverse section of adult cadaver through the symphysis mandible and the epiglottis. Superior view.

The alar fascia extends across the midline posterior to the pharynx, esophagus, and visceral fasciae, and fuses with the prevertebral fascia at the tips of the transverse processes to which both these layers are attached. It then passes anterolaterally to form the medial wall of the carotid sheath, fusing with the sternothyroid layer and the deep surface of the sternocleidomastoid sheath. It also forms the posterior and lateral walls of the carotid sheath, again fusing with the deep surface of the sternocleidomastoid sheath and thus forming a complete sheath of alar fascia, the carotid sheath. Posteriorly, between the transverse processes, the alar fascia extends from the base of the skull to about the level of the seventh cervical vertebra, where it becomes intimately fused with the visceral fascia. (Figs. 1-7.)

The prevertebral layer lies just anterior to the bodies of the vertebrae from the base of the skull to the coccyx. In the neck it extends laterally to the tips of the transverse processes where it is fused both to these processes and to the alar fascia. Lateral to the transverse processes, it becomes the scalenus fascia which forms the sheaths of the scaleni, splenius capitus, levator scapulae, and the other deep muscles of the back of the neck, and finally attaches to the spines of the vertebrae. Inferolaterally the scalenus fascia, after giving origin to the axillary sheath enclosing the axillary vessels and brachial plexus, attaches to the first and second ribs. In the thoracic and abdominal regions, the lateral extension of the prevertebral fascia becomes the extrapleuroperitoneal or transversalis fascia. Over the dome of the pleura, it is identical with the layer often described as Sibson's fascia. (Figs. 1-7.)

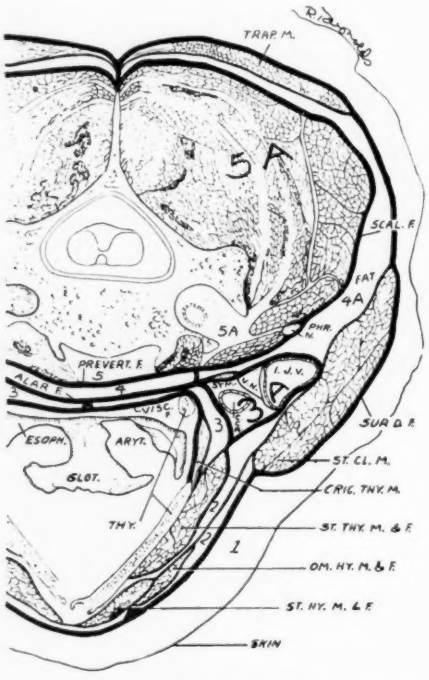

Fig. 6.—Transverse section of adult cadaver at the level of the thyroid cartilage. Superior view.

Fascial Spaces.—The superficial space (1) is the potential space between the skin and deep fascia; that is, within the superficial fascia. It is the seat of superficial cellulitis and is continuous from region to region; in this case, from head to neck and trunk. In the neck it may be subdivided into superficial and deep portions by the platysma muscle, both divisions being fairly loose and allowing rather large accumulations of fluids. (Figs. 1-8.)

Deep Fascial Spaces: These may be considered under two headings: those of the infrahyoid region and those of the suprahyoid region. For

convenience we have roughly divided the infrahyoid spaces into those of the anterior and posterior triangles, the former being designated by numerals and the latter by corresponding numerals followed by the letter *A*.

Of the infrahyoid spaces, Space 2 is the potential space between the superficial layer of deep fascia and the deep layer of the sternothyroid-thyrohyoid sheath. It contains, therefore, the sternohyoid-omohyoid muscles with their sheaths and the sternothyroid-thyrohyoid muscles with the anterior layer of their sheaths. The extent of the space was demonstrated by injections of gelatin colored with India ink, as well as by study of dissections and sections. It is continuous across the midline and is blind laterally where the sternohyoid and sternothyroid layers

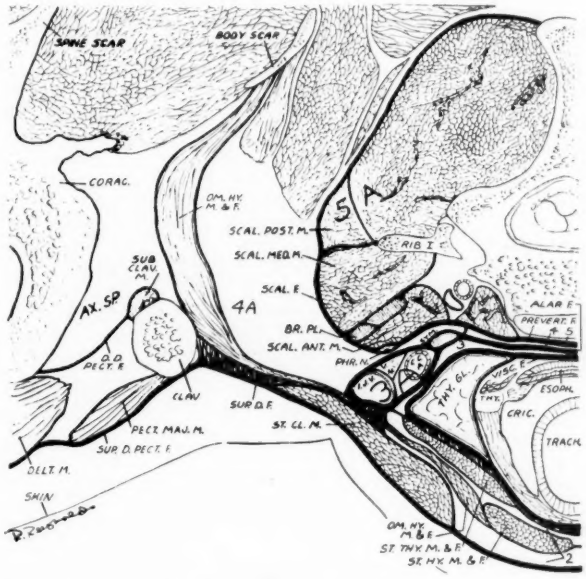

Fig. 7.—Transverse section of adult cadaver through the root of the neck. Superior view.

fuse to the deep surface of the sternocleidomastoid. It is also blind superiorly at the hyoid bone, superolaterally along the superolateral border of the anterior belly of the omohyoid, and inferiorly at the sternum and clavicle. The most frequent extensions of injected masses from this space were along the pulley of the omohyoid to Space 2*A*, superficially into Space 1, and deeply into Space 3. (Figs. 1, 2, 6-8.)

Space 2*A*, between the superficial layer of deep fascia and the sheath of the posterior belly of the omohyoid muscle, is blind anteriorly at the pulley, posteriorly at the insertion of the omohyoid (posterior belly), posterosuperiorly along the posterosuperior border of that muscle, and inferiorly at the clavicle. The most common extensions from this space were along the pulley into Space 2, and into Spaces 1 and 4*A*. (Fig. 7.)

Space 3 is the potential space between the visceral fascia on the one hand and the sternothyroid layer, carotid sheath, and alar fascia on the other. It thus has anterior, lateral, and posterior portions, all continuous. On the posterior side, it extends from the base of the skull to the level of the seventh cervical vertebra, where it is shut off by the close fusion of the visceral and alar layers. On the anterior side, it extends from the thyroid cartilage to the upper border of the arch of the aorta (fourth thoracic vertebra), where it is shut off by dense adhesions between the fibrous pericardium and the sternum. Laterally, this space is blind at the root of the neck where there are dense adhesions between the alar and visceral fasciae around the inferior thyroid arteries. Injected masses tended to remain localized within Space 3, but, when spread did occur, it was usually into Spaces 2, 4, and inferiorly into the superior mediastinum slightly lower than the normal limits of the space. This is of special importance in Ludwig's angina. (Figs. 1-7.)

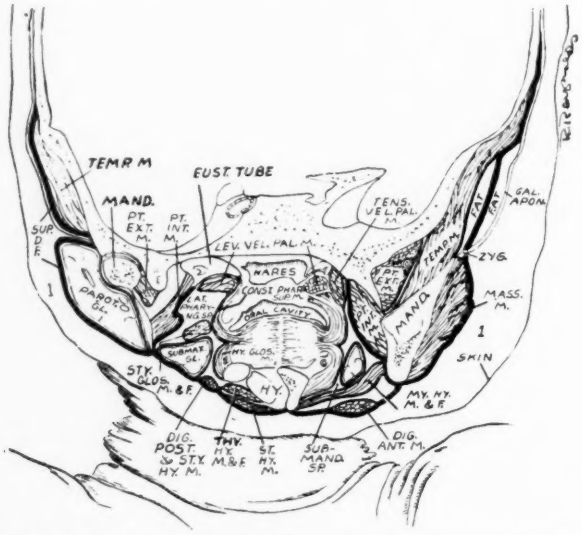

Fig. 8.—Frontal section of full term fetus through base of tongue and posterior nares. Anterior view.

Space 3A is the potential space within the carotid sheath. Primary injections into this space were usually limited closely to the region of injection, but in some cases the masses extended as high as the hyoid bone and as low as the root of the neck, beyond which levels the close adherence of the sheath to the contained structures made further spread impossible. The space therefore bears little relation to infections of the head and neck except those associated with thrombosis within the internal jugular vein and with the lymph nodes lying within the sheath. (Figs. 2-7.)

Space 4, often referred to as the "danger space," is the loose areolar space between the alar and prevertebral fasciae. It is limited laterally where these layers fuse at the tips of the transverse processes. It extends superiorly to the base of the skull and inferiorly into the posterior

mediastinum. It is because of the latter relationship that it is often called the "danger space." There was very little tendency for injected masses to spread beyond this space, the most common being into Space 4*A*. However, extension did occur from other spaces into this space, especially from Space 3. It is in this way that Ludwig's infection and retropharyngeal abscesses find their way into the posterior mediastinum. (Figs. 1-7.)

Space 4*A* is the potential space between the superficial layer of deep fascia and the scalenus fascia. In the subclavian triangle it lies between the sheath of the posterior belly of the omohyoid muscle and the scalenus fascia. This space is continuous with the axilla, but a rather dense fatty pad between the clavicle and the first rib makes this communication less free. (Figs. 2-7.)

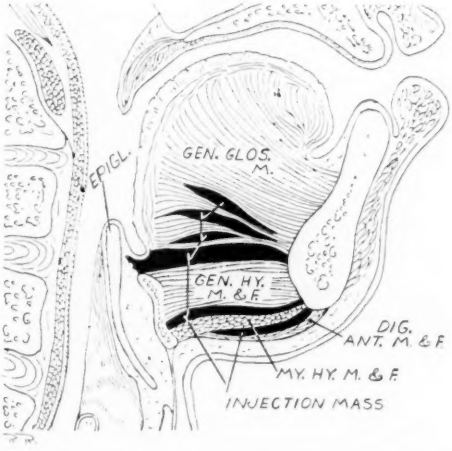

Fig. 9.—Diagrammatic drawing of median sagittal section showing the collection of injection masses between submental muscles and particularly the extension of the mass between the genioglossus and geniohyoid muscles toward the epiglottis.

Space 5 is the potential space between the prevertebral fascia and the bodies of the vertebrae. It extends from the base of the skull to the coccyx and is limited laterally by the attachment of the prevertebral fascia to the transverse processes. This is the space involved in tuberculosis of the vertebral bodies, resulting in cold abscesses which extend inferiorly along muscles taking origin from the vertebral bodies (psoas abscess). There was very little tendency for injected masses to rupture through the walls of this space into Spaces 4, 4*A*, and 5*A*. (Figs. 1-7.)

Space 5*A*, posterior to the scalenus fascia, lies between the deep muscles of the back of the neck. Infections within it extend superiorly and inferiorly along these muscles, thus sometimes traveling great distances. (Figs. 2, 4-7.)

In the suprahyoid region are the masticator, temporal, parotid, lateral pharyngeal and submandibular spaces. The masticator space is bounded by the superficial layer of deep fascia which, after form-

ing the sheath of the masseter muscle, passes around the anterior and posterior borders of the ramus of the mandible and becomes continuous with the sheaths of the pterygoid muscles. The space thus contains the masseter muscle, the external and internal pterygoid muscles, and the ramus of the mandible. It is closed on all sides except superiorly, where it is in relation with the temporal space, deep to the deep temporal fascia. Injections into either space spread to the other and, under increased pressure, ruptured either superficially through the masseter sheath or deeply into the parotid space or lateral pharyngeal and submandibular spaces. The parotid space was found to be a completely closed space formed by a split of the superficial layer of deep fascia and occupied by the parotid gland, external carotid artery, and posterior facial vein. Injections into this space showed infiltration into the substance of the gland and ruptures through the capsule; superficially with subcutaneous collections and deeply with extensions into the masticator, lateral pharyngeal, and submandibular spaces. Such collections in the submandibular space could in the later stages resemble Ludwig's angina even though the original infection was far removed from the floor of the mouth. (Figs. 3, 4, 8.)

The lateral pharyngeal space is an important fascial space of the head which is bounded by the pharynx, medially; the styloid muscles and carotid sheath, posteriorly; the parotid gland, posterolaterally; the mandible, pterygoids, and masseter, anterolaterally; and the pterygomandibular raphe, anteriorly. Superiorly, it extends to the base of the skull and, inferiorly, it is shut off from the neck by the attachment of the submaxillary capsule to the sheaths of the stylohyoid and the posterior belly of the digastric muscles. Inferomedially, it communicates freely with the submandibular space deep to the submaxillary capsule. Posteromedially, it communicates with Space 3. Injections made through the palatine tonsil and lateral pharyngeal wall went directly into the lateral pharyngeal space. From here, the injected masses spread easily into Space 3 and, in some cases, ruptured through the alar fascia into "danger space" 4. Extension into the submandibular space took place freely. The lateral pharyngeal space is therefore infected from tonsillar abscesses, from retropharyngeal abscesses involving Space 3, and secondarily from the floor of the mouth through the submandibular space. Likewise, infections in this space may spread to the submandibular space and, in the later stages, resemble true Ludwig's angina. (Figs. 3-8.)

The submandibular space is most important in the consideration of Ludwig's angina. We have coined the term submandibular space to include the regions of the submental and submaxillary triangles lying between the mucous membrane of the floor of the mouth and the superficial layer of deep fascia over these regions. It thus encloses the sublingual and submaxillary salivary glands (the latter in a complete capsule), the genioglossus, geniohyoid, mylohyoid, and digastric (anterior belly) muscles. The floor or deep wall of this space is made up of the

hyoglossus and superior pharyngeal constrictor muscles, the latter covered by visceral fascia. Thus, a group of potential spaces, all communicating, is established between the submental muscles, crossing the midline and extending deep to the capsule of the submaxillary salivary gland, superolaterally, to become continuous with the lateral pharyngeal space. This group of spaces, collectively making up the submandibular space, is limited inferiorly at the hyoid bone where the submental muscles and their sheaths attach; and inferolaterally at the inferior borders of the stylohyoid and posterior belly of the digastric muscles, the sheaths which are attached to the superficial layer of deep fascia superficially and the carotid sheath deeply. (Figs. 3, 5, 8.)

Injections made through the mucous membrane of the floor of the mouth anywhere from the midline anteriorly to the anterior tonsillar pillar posteriorly passed into the submandibular space. The more anterior injections first passed between the submental muscles and then spread laterally toward the lateral pharyngeal space deep to the submaxillary salivary gland. The more posterior injections passed into the lateral pharyngeal space more quickly. From the lateral pharyngeal space, the injections often passed into Space 3, from where they sometimes spread to the superior mediastinum or broke through the alar fascia and extended down Space 4 to the posterior mediastinum. A similar extension of infection is one of the causes of fatal outcome in Ludwig's angina. In addition, there was usually submucous extension within the floor of the mouth, forming, with sufficient pressure, a horseshoe-shaped elevation around the base of the tongue and extending back as far as the tonsillar pillars, pharynx, and larynx. A similar spread of infection and the accompanying swelling give the basis for the anginal symptoms in Ludwig's angina, often sufficient to produce fatal suffocation. The commonest rupture through the walls of the submandibular space was through or around the submaxillary capsule to the superficial tissues (Space 1) of the neck and face. Deeper breaks occurred laterally into the sheath of the sternocleidomastoid muscle and inferiorly, through the attachment of the stylohyoid and digastric sheaths to the carotid sheath, into Spaces 2 and 3 along the sternothyroid and sternohyoid muscles. These extensions account for the swelling in Ludwig's angina extending to the clavicle and up over the face. A fairly common extension was between the genioglossus and geniohyoid muscles posteroinferiorly to the region of the epiglottis where the mass appeared submucously (Fig. 9). A similar spread of infection would certainly be an important cause of edema of the glottis which is often the cause of death in Ludwig's angina.

ETIOLOGY

The great majority of cases of true Ludwig's angina originates from carious teeth, the infection of which erodes through the thinnest portion of the mandible. Since this is on the anterior (labial) side for the front teeth and buccal side for the back teeth (molar and premolar), the localization is superficially at the gums for the former, but deeper in

the sublingual tissues, related to the mandibular canal, for the latter (Moty, 1892; Novitzky, 1935). The result is a spreading cellulitis along the routes already described (Figs. 1-9). A similar infection may result from scratches and wounds of the mucous membrane of the floor of the mouth, allowing direct access of pathogenic bacteria. The latter are usually the common pyogenes, streptococci, and staphylococci, but other mouth inhabitants such as Vincent's organisms and the spirochete group may be primary or secondary invaders. The majority of cases of true Ludwig's angina occurs in adults. Those cases described as occurring in infants and children no doubt originate in the nose and throat, spread by lymphatics, and are not true cases of Ludwig's angina.

CLINICAL COURSE

Following a history of swelling of the gums about the lower molar teeth which may or may not be accompanied by pain, the patient develops a fever which may be preceded by a chill. The temperature may vary from 99 to 105° F. An external swelling soon appears. This at first involves only the submaxillary triangle on that side or may start in the midline in the submental region; but, if not treated promptly, it soon spreads across the midline to the other side, superiorly over the face, and inferiorly to the sternum and clavicle. The submaxillary and submental swelling is characteristically "woody" hard, indicating the presence of deep inflammatory reaction under pressure, with or without free pus. The extensions superiorly and inferiorly may be superficial or deep according to the points of rupture through the walls of the submandibular space. The patient experiences difficulty in opening the mouth. The floor of the mouth becomes swollen and indurated; the tongue becomes swollen and elevated so as to touch the roof of the mouth and block the fauces. The respirations may become difficult and labored. If no relief is obtained, death results from suffocation due to the swelling of the floor of the mouth and tongue, or edema of the glottis, or both; or from mediastinitis, the spread occurring from the submandibular space to the lateral pharyngeal space and then to Spaces 3, or 4, or both, as indicated above (Figs. 1-9). Death also may occur from septicemia or aspiration pneumonia.

There is considerable variation in the acuteness and virulence of these cases, some being very fulminating and rapidly fatal and others of less severity or relatively benign.

TREATMENT

The sheet anchor of treatment consists in early and adequate drainage. Since death usually results from suffocation due to pressure or from extension of the infection to the mediastinum, it is obvious that early and proper incision offers the best hope of relieving pressure and preventing extension of the infection. Incision may be made vertically in the midline, or transversely below the body of the mandible, or a com-

bination of the two may be used. The midline incision is indicated in obvious collections in the submental region, but often it fails to drain adequately more laterally lying collections. The lateral incision is more effective in the majority of cases and may be well combined with the median incision. In any event, the opening must be carried deeply to the mucous membrane of the floor of the mouth. Little or no pus may be obtained but beneficial release of pressure will result, and pus may appear in the wound a little later. In the midline the incision passes between the submental muscles of each side—anterior belly of the digastric, mylohyoid, geniohyoid, and genioglossus—a separation being made laterally in each plane to drain that particular level. In the lateral incision the procedure must include the displacement or excision (Rehn, 1922; Linsay, 1923-4; Colp, 1933; Ramsdell, 1934) of the submaxillary salivary gland, incision through the mylohyoid muscle, and separation of the muscle planes medially. A combination of sharp and blunt dissection is safest. (Figs. 1, 3, 5, 8.)

CASE REPORTS

CASE 1.—A. G. (University Hospital No. 54086), male, aged 17 years, was admitted with high temperature (105° to 106° F.), rapid pulse (120 to 150), and delirium. Nine days previously he had suffered a severe chill followed by high fever which subsided two days later. His only complaint at this time was backache. The next day his temperature rose to 104° F. and he complained of pain in the left knee. Five days later he complained for the first time of toothache on the right side; his temperature rose to 105° F. and he became delirious. The day before entrance, six upper and lower right molar and bicuspid teeth were removed, the teeth being loose and described as being "just lifted right out."

Physical examination showed a well-developed young man, acutely ill and in a semicomatose state. There were six bleeding sockets of recently extracted teeth in the right lower and upper jaws. There was moderate swelling of the submaxillary triangle and some swelling over the left sternoclavicular joint.

Laboratory examination: Red blood cells, 4,650,000; Hgb., 84 per cent; and white blood cells, 24,650. Urine showed 2+ albumin. Blood culture positive for hemolytic *Staphylococcus aureus.*

Course: Patient was given a transfusion of 500 c.c. of blood and supportive treatment, but died day after admittance.

Autopsy: Osteomyelitis of right maxilla and mandible with extension by continuity to submandibular space, Space 3, and the superior mediastinum. Metastatic abscesses in left sternoclavicular joint, chest wall, and most of internal viscera.

Comment.—This case presents the picture of a rapidly spreading infection, starting in the lower right molar and bicuspid teeth, extending through the floor of the mouth by continuity to the submandibular space, from there rapidly into Space 3, and then inferiorly into the superior mediastinum. The rapidity of the spread and absence of an inflammatory wall were no doubt responsible for the absence of marked swelling of the floor of the mouth and of anginal symptoms. Meanwhile the infection invaded the blood stream and gave rise to numerous metastatic abscesses.

CASE 2.—C. H. (University Hospital No. 31713 and No. 32160), male, aged 23 years, entered the hospital complaining of painful swelling under left side of lower jaw, inability to open his mouth, and fever. Illness began four weeks previously with a swelling below the angle of the lower jaw which was not painful during the first week, but which became progressively more painful until a few days before entrance when there was a sudden additional increase in pain and swelling. Since the onset, it had become more and more difficult for him to open his mouth.

Examination on entrance showed a swelling on the left side of the face and neck involving chiefly the submaxillary triangle, but extending over the body and ramus of the mandible superiorly and halfway to the clavicle inferiorly. The swelling was firm, indurated, and moderately tender. The jaw could not be opened. The temperature was 101° F., pulse 80, and respirations 22. The teeth could not be examined on account of inability to open the mouth, but patient gave history of long-standing tooth pathology.

Laboratory findings: White blood cells, 10,800, with 72 per cent polymorphonuclears. X-ray showed osteomyelitis of jaw below left second and third molar teeth.

Course and treatment: On the day after admission external incision was made through a small area of fluctuation in the submaxillary swelling and a rubber drain inserted. Free pus was obtained which showed *Staphylococcus aureus* on culture. Six days later three additional incisions were made in the neck for drainage. Eight days later the jaws were pried open and the lower left second and third molars were removed. One week later incisions were made over the ramus of the mandible and lower in the neck for drainage purposes. A few days later the patient was dismissed from the hospital, improved. He was readmitted to the hospital one week later and an incision was made over the ramus of the mandible from the ear to the level of the thyroid cartilage. No free pus was obtained. One month later an additional incision was made posterior to the previous one. A small amount of free pus was obtained. Final operation was done one week later with incision posterior to former incisions, wide exposure, and blunt dissection deeply. From this time on, patient made a gradual recovery and left the hospital with wounds almost healed three weeks after readmission.

Comment.—This case presents a picture of true Ludwig's angina of moderate virulence, starting, as usual, from carious lower molar teeth and extending to the submandibular space from the floor of the mouth. The infection broke through the deep fascia and spread superficially over the face and lower neck. It also spread posterosuperiorly to the lateral pharyngeal space. There was apparently no mediastinal involvement. There was the usual swelling in the floor of the mouth and difficulty in opening the jaw. The numerous operations are evidence of a failure to appreciate the anatomic spaces and tissues involved, and of the resulting insufficient and unwisely placed incisions for drainage, although recovery eventually ensued.

CASE 3.—E. A. (University Hospital No. 60437), male, aged 23 years, entered the hospital complaining of swelling and pain of the right lower jaw, of six weeks' duration. Patient had a cold six weeks before entrance, which was improving when his right jaw, neck, and face swelled suddenly, over night. There was progressive difficulty in opening the mouth. Two days previous to onset of the swelling, he had consulted his dentist on account of pain and swelling over a nonerupted lower right wisdom tooth. The dentist "seared" the gum with an electric needle. About two weeks later, the wisdom and first molar teeth (lower right) were extracted under ether anesthesia in a local hospital, and he was discharged after ten days with the

external swelling well down but the gum still swollen. There was some drainage from a small skin incision over the angle of the jaw, made at the time of extraction. The external swelling with associated pain returned three days after discharge from the hospital. The external wound margins were spread and the patient was sent to the University Hospital.

Examination on entrance showed a hard, indurated swelling of the right submaxillary region extending superiorly over the mandible and inferiorly to about the level of the thyroid cartilage. It was very tender. Thick, yellow pus could be expressed from the small incision over the angle of the jaw. Culture showed *Staphylococcus aureus*. Temperature was 100° F., pulse 92, and respirations 15.

Laboratory findings: White blood count 8,600 with 48 seg. and 30 staff. X-ray showed rarefaction, about 2 by 4 cm. in area, in the right side of the body of the mandible under the extracted molar teeth, with questionable sequestration.

Course and treatment: Two additional small incisions were made, one over the body of the mandible and the other below the body of the mandible. There was rather free drainage of pus with reduction in the swelling and pain. The temperature and pulse are now practically normal, but I doubt if the patient will avoid further surgery, in view of the sequestration and the small inadequate incisions.

Comment.—This is a rather typical history of Ludwig's angina of moderate virulence treated inadequately by small incisions, unwisely placed. The treatment has been sufficient to control the original acute symptoms and prevent dangerous spread to the mediastinum, but insufficient to give prompt and complete recovery.

CASE 4.—R. V. (University Hospital No. 56297), female, aged 21 years, entered the hospital complaining of swelling and pain of the right lower jaw, fever, and difficulty in swallowing. Two days previously she noted a painless swelling in the region of the lower right, third molar tooth. Her dentist refused to extract until the swelling subsided. The swelling then became very painful, and the patient experienced difficulty in opening the mouth and swallowing. The day before entrance she had a severe chill and rise in temperature.

Examination on entrance revealed an indurated, boardlike swelling over the right submaxillary region, which extended across the midline anteriorly, over the angle of the jaw to the ear superiorly, and to the clavicle inferiorly. The mouth could be opened just 1 or 2 cm., revealing a swollen floor and an elevation of the tongue. The throat could not be visualized. Temperature was 104° F., pulse 96, and respirations 22. X-ray showed an area of rarefaction about the right lower second and third molar teeth (the latter impacted).

Course and treatment: The first operation, performed the day after entrance, consisted of removal of the lower right second and third molar teeth with establishment of internal drainage, care being taken to prevent aspiration of blood and pus into the lungs. In the second operation, done four days later, a midline incision was made through the skin and superficial fascia and the deeper structures were separated with a hemostat down to the floor of the mouth, releasing thick, foul-smelling pus. The third operation was done two weeks later with incision transversely to the right and below the previous midline incision. No free pus was obtained. There was gradual reduction in temperature, swelling, and induration. Patient was dismissed fully recovered.

Comment.—The above case presents a rather typical case of Ludwig's angina treated adequately by internal and external drainage. The internal and midline external drainage was effective in reducing the swelling and causing a subsidence of the general symptoms, but the appear-

ance or persistence of an indurated area farther laterally made an additional lateral incision necessary. Although no free pus was obtained here, the result was to hasten the convalescence and final recovery.

SUMMARY AND CONCLUSIONS

1. Ludwig's angina is a clinical entity resulting from spread of infection from the floor of the mouth by fascial planes.

2. The spread from the floor of the mouth occurs into the submandibular space, deep to the superficial layer of deep cervical fascia. Further spread may take place by rupture through the walls of this space superficially into the face and lower neck (Space 1), or deeply into the neck (Spaces 2 and 3).

3. Extensions may occur from the submandibular space deep to the submaxillary gland capsule to the lateral pharyngeal space. From here, the infection may spread to Space 3 by direct continuity, or through the alar fascia to the danger Space 4. From Space 3 the infection may extend to the superior mediastinum and from Space 4 to the posterior mediastinum.

4. Death from Ludwig's angina occurs either from suffocation due to edema of the floor of the mouth, tongue, and glottis; or from mediastinitis due to spread through the above mentioned spaces. Septicemia and aspiration pneumonia may be terminal.

5. The usual foci are the lower molar or bicuspid teeth, although scratches or wounds in the mucous membrane of the floor of the mouth may be the portals of entry.

6. Streptococci and staphylococci are the commonest organisms responsible, but Vincent's organisms and the common spirochetal inhabitants of the mouth may be primary or secondary invaders.

7. Infections starting from the nose and throat may spread into the retropharyngeal and lateral pharyngeal spaces or may extend into the neck by lymphatics. They should not be classified as cases of true Ludwig's angina, although they may resemble it in their later manifestations.

8. The clinical characteristics of true Ludwig's angina include constitutional symptoms (chills, fever, etc.) and local findings. The latter consist of boardlike swelling of the neck centering about one or both submaxillary triangles and the submental triangle (submandibular space), elevation of the floor of the mouth and tongue, and difficulty in opening the mouth, speaking, and swallowing.

9. Treatment consists of adequate and proper surgical drainage, instituted as soon as the diagnosis is made.

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THE SURGERY OF THE TEMPOROMANDIBULAR JOINT

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AS COMPARED with other joints in the body, the temporomandibular joint is in many ways unique. It is a small joint which is in constant use, is frequently traumatized, and, yet, on the whole, is subject to few pathologic lesions requiring surgical interference. The joint itself is a complicated one, owing to the fact that it contains an interarticular fibrocartilage which divides the joint cavity into two separate compartments (Fig. 1). In the upper joint a gliding movement occurs, while in the lower, the movement is of a hinge character. The interarticular disk is of great importance for it may be torn or dislocated as the result of trauma. The disk itself is a thin, oval plate of fibrocartilage, the fibrous tissue predominating to such extent that in many cases in which I have excised the disk no cartilage cells have been visible under the microscope.

The upper surface of the disk is concavoconvex from before backwards, to accommodate itself to the form of the articular fossa and articular eminence on the temporal bone. The under surface, which is concave, is moulded onto the rounded head of the mandible. The capsular ligament of the joint is adherent to the circumference of the disk and the upper part of the tendon of the external pterygoid muscle is attached to its anterior part. The attachment of the external pterygoid muscle is of practical importance, for in such cases of dislocation of the joint the interarticular disk follows the condyle of the mandible.

DISLOCATION OF THE JOINT

Owing to the stability of the joint and its protection by the overlying temporal muscle, dislocation is uncommon. In an analysis of 38 cases of forward dislocation of the jaw seen during the last twenty years, it

TABLE I

CAUSATION	MEN	WOMEN	TOTAL
Boxing bouts	20	0	20
Dental extractions	5	4	9
Use of gag during anesthesia	4	1	5
Laughing	0	1	1
Yawning	1	2	3
Total	30	8	38

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is interesting to note that only 2 developed recurrent dislocations and even these did not require any surgical intervention.

The causation of the dislocation is outlined in Table I.

This brings out the fact that boxing bouts, where a punch is directed to the point of the chin when the mouth is open, is the commonest cause of dislocation in men, while in women the commonest cause is dental extractions, especially where an attempt is made to elevate an unerupted third mandibular molar.

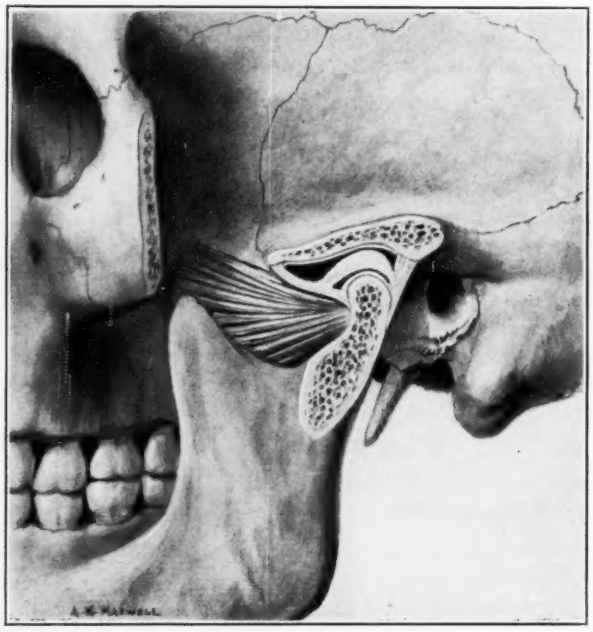

Fig. 1.—Section of the temporomandibular joint, showing the size and position of the articular disk.

The mechanism of forward dislocation is quite simple; the condyle of the mandible slips over the articular eminence (Fig. 2) into the zygomatic fossa of the temporal bone. The dislocation is usually bilateral, but may be unilateral, depending on the exciting cause; those due to dental extractions are mostly unilateral.

Reduction of the dislocation is easily carried out, and, as a rule, does not tend to recur owing to the fact that the muscles and periarticular structures are not weakened by the dislocation. Unreduced dislocations are rarely seen, and, when present for a long time, a false joint may result. In one case which came under observation, a gipsy woman, aged 76 years, had suffered from a dislocated jaw for twenty years, the dislocation being due to a bad dental extraction by another gipsy who used a pair of motor pliers to remove a lower molar tooth. The dislocation was unilateral and well-marked false joint had formed. The disability appeared slight, but talking was difficult.

DISPLACEMENT OF THE ARTICULAR DISK

This is an uncommon accident, but a much more difficult condition to treat than dislocation of the joint.

Displacement of the disk may be caused by a violent cough, sneeze, or yawn, especially when the pterygoid muscles are contracted, as occurs

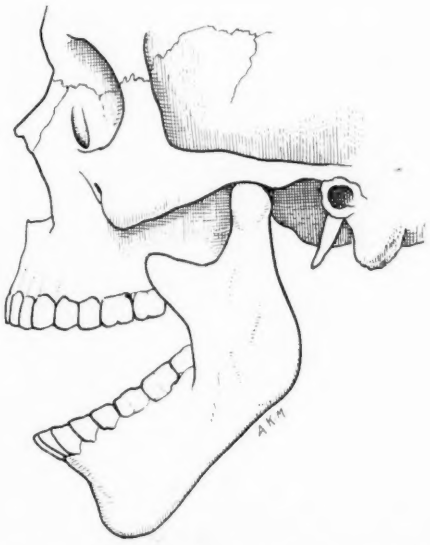

Fig. 2.—Forward dislocation of the mandible, showing the relation of the condyle to the articular eminence.

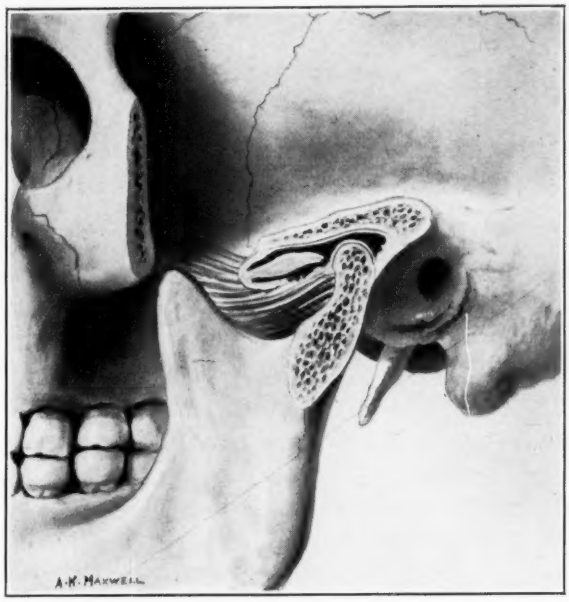

Fig. 3.—Section through the temporomandibular joint, showing the displaced articular disk. The action of the external pterygoid muscle is partly responsible for this, as can be seen in the drawing.

when trying to prevent a cough, sneeze, or yawn. Occasionally, displacement may result from a blow on the jaw when the mouth is open, the trauma not being of sufficient force to cause dislocation of the condyle over the articular eminence of the temporal bone.

Fig. 4.—X-ray of a normal temporomandibular joint.

The posterior thinned-out part of the disk becomes detached from the capsule, which permits it to be drawn forward and inward by the external pterygoid muscle, and, as the mouth closes by elevation of the jaw, the disk of cartilage becomes severely crushed between the condyle and the glenoid fossa of the temporal bone (Fig. 3). The symptoms which result from such a displacement are quite characteristic. In some cases the patients volunteer the remark that they heard something snap in the ear. Sudden acute pain starting in the joint and referred to the pinna or the skin above it is a constant symptom. The auriculotemporal nerve is responsible for the referred pain, as it not only supplies the joint but the pinna and the scalp in the temporal region as well. Excessive salivation is often quite a marked feature, owing to the stimulation of the nerve. Owing to the pain, the patient is unable to close the mouth and mastication is almost impossible. In all cases of

displacement of the disk a synovitis is set up and this condition is to a certain extent responsible for the pain. Sometimes an x-ray picture of the joint may be of use in demonstrating the displaced disk (Figs. 4 and 5). Both temporomandibular joints should be x-rayed in order that a comparison may be made. On the side of the displacement a much larger joint space is seen when compared with the normal side. Reduction of the displacement is performed by exerting continual pressure behind the condyle of the jaw while the mouth is open. By this

Fig. 5.—X-ray of a case in which the articular disk has been displaced. Note the great increase in the joint space as compared with that shown in Fig. 4.

method the convex upper part of the condyle will be insinuated into the concave lower surface of the articular disk. Generally speaking, after a few minutes of continued pressure, the mouth is closed by gradually elevating the jaw. In some cases the disk slips back with quite an audible click, while in others the patient experiences a movement within the joint and is suddenly aware of the removal of all obstruction

to free movement. To obtain this reduction quickly is a knack which can only be attained by experience; the surgeon may have to make several attempts before the disk is replaced to its normal position.

In those cases where the condition becomes chronic and repeated or almost continuous displacement occurs, there is a tendency for the disk to cause a "snapping" sound, every time the mouth is opened. This snapping is most noticeable during mastication and may become a source of great annoyance or embarrassment to a female patient or her friends. The psychologic effect of a snapping joint may be very marked, especially in females. They become introspective and nervous and are afraid to have meals in public.

It is the chronic cases, for the most part, which come under the surgeon's care, but not until every other form of treatment has been tried. Quite a number of these cases have been treated by osteopaths without any success. There is only one form of treatment which provides a permanent cure and that is excision of the articular disk, which cannot be looked upon as a very serious surgical procedure. The joint can best be exposed by means of a T-shaped incision, the edges of the wound being kept open by means of a small self-retaining retractor. On opening the joint capsule, the displaced articular disk is found in the anterior part of the joint. The disk is generally quite loose and can be removed entirely by cutting through its anterior connections with a knife. The capsule is then to be closed by two or three interrupted catgut sutures, and the skin approximated by a few silkworm-gut sutures. A four-tail bandage is applied to the lower jaw and after full recovery from the anesthetic the patient is encouraged to open the mouth and so gain confidence that this movement can be undertaken without pain or snapping. The patient is allowed up on the second day and discharged from hospital at the end of a week, after the skin stitches have been removed. It might be thought that after excision of the articular disk the joint might not be stable and that the movements might be excessive with a tendency for forward dislocation of the jaw to take place, but this is definitely not the case. In some twenty cases recently examined at King's College Hospital in the follow-up clinic, the results were excellent both from the functional and anatomic standpoints, while all the patients were delighted with the result of the treatment. Some of the cases were operated upon more than fifteen years ago.

The whole profession realizes the excellent results which follow excision of the medial meniscus of the knee joint after it has been torn, but there seems to be a tendency for many physicians to remain sceptical with regard to excision of the articular disk of the temporomandibular joint, and to recommend their patients to continue with diathermy and other forms of treatment for years.

ACUTE ARTHRITIS OF THE JOINT

This condition is relatively more common than is thought to be the case. It may follow scarlet fever, typhoid fever, gonorrhea, dento-alveolar abscess, acute parotitis, and rarely, acute mastoiditis, when inflammation spreads forward into the zygoma owing to the involvement of the air cells in this region. The surgeon is rarely called upon to deal with acute arthritis of the joint except in those cases in which suppuration takes place, and an incision is required to liberate pus. He is consulted, however, when ankylosis of the joint has occurred and the patient seeks relief from the disability therefrom.

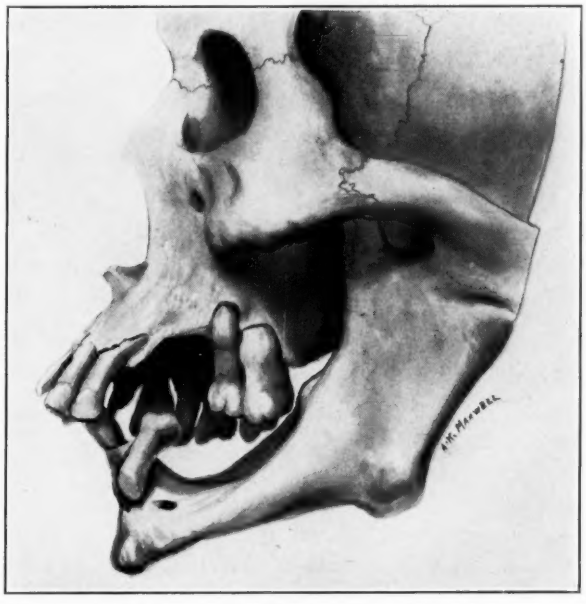

Fig. 6.—Ankylosis of the temporomandibular joint of many years standing (Royal College of Surgeons Museum).

ANKYLOSIS OF THE JOINT

When ankylosis occurs, the articular disk disappears and the whole surface of the glenoid fossa of the temporal bone and the upper surface of the condyle of the mandible become completely fixed (Fig. 6). It is not generally recognized how extensive and how firm is this bony ankylosis. On this account any relief or cure of the condition must be properly planned. Any attempt to divide the bony surfaces with a hammer and chisel will only result in an extensive fracture of the base of the skull with the possibility of meningitis as a further complication.

In a series of cases which have come under my supervision during the last twenty-five years in which a variety of surgical procedures have been performed, the ultimate results have been assessed, and now it may be said that crystallization of thought in treatment has occurred.

It must be remembered that excision of the head of the mandible for ankylosis is quite an old procedure, being first performed by Professor Humphrey, of Cambridge, in 1856. Many successful cases have been reported from time to time, but how many bad results have never been published? That no stable operative technique has so far been established is proved by the fact that over a dozen different types of operation have been reported. The first difficulty that occurs is the size and shape of the incision, because there must of necessity be a limited approach owing to the important structures in the neighborhood of the facial nerve and on the medial side the internal maxillary artery (Fig. 7). A T-shaped incision over the joint gives the best exposure and

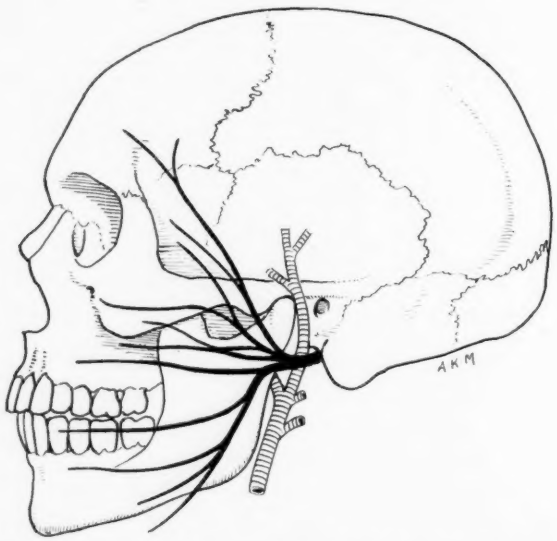

Fig. 7.—Drawing showing the relations of the facial nerve, the internal maxillary, and the superficial temporal artery to the temporomandibular joint.

does not damage any of the structures in the immediate neighborhood of the joint. The neck of the condyle is exposed and a fine Gigli saw is passed round it. The bone is then easily divided with a minimum of trauma. By means of a small pair of curved nibbling forceps, some of the bone constituting the condyle of the mandible is carefully removed. Next a dental burr is used to obliterate and flatten out the massive bone formation constituting the ankylosed joint. In my opinion it is the use of the dental bone burr which has established this operation as there is no likelihood of damage to the external auditory meatus or to the middle fossa of the skull.

When a conveniently large cavity has been made in the region of the joint, the exposed bony surfaces are rubbed with bone wax to prevent any oozing of blood and also to prevent any new formation of bone. Having tried a variety of different substances to cover the exposed surface of the neck of the condyle, I have come to the conclusion that the

patient's living tissues in the shape of muscle tissue is far the best. Celluloid, cargile membrane, and chromatized pig bladder have all been in vogue at one time or another, but the human body does not tolerate

Fig. 8.—The use of a portion of the posterior part of the temporal muscle after excision of the temporomandibular joint.

Fig. 9.—The employment of some fibers of the masseter muscle after excision of the temporomandibular joint for ankylosis.

foreign tissue kindly. Simple procedures should always be advocated in place of difficult and complicating ones if they give the same results. It is quite easy to make use of a portion of the temporal muscle or a portion of the masseter muscle (Figs. 8 and 9), without affecting in the least the action and strength of the muscle itself.

The follow-up of these cases has been most instructive, for during the first year after operation there is no doubt that female patients make more rapid progress than male, and it is during this period that encouragement is required and some occasional diathermy treatment to the muscles in the neighborhood of the joint should be given. The results should not be assessed until at least six months after the operation when both surgeon and patient are quite pleased with the result. It must be remembered that quite often the ankylosis has been present for a long time and the muscles surrounding the joint have undergone atrophy from disuse. The re-education of these atrophied muscles takes a considerable time.

Age is no contraindication as some patients over the age of 80 years have been successfully operated upon. In infants, however, if they can be fed, it is better to postpone the operation until after 6 years of age, owing to the smallness of the joint.

In a few cases congenital ankylosis has been reported, but as Gladstone and I reported in 1923, antenatal defects of development appear to be the result of the same conditions which, in some subjects, may produce defect in growth, after as well as before birth. We believe that the defects in the growth of the face and lower jaw are usually associated etiologically with defective development of the brain.

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THE TREATMENT OF THROMBOPHLEBITIS OF THE DEEP VEINS OF THE LOWER EXTREMITIES WITH INTERMITTENT VENOUS OCCLUSION

A Preliminary Report

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INTRODUCTION

COLLENS and Wilensky[1] in 1936 reported the results of the use of intermittent venous occlusion in the treatment of certain types of peripheral vascular disease. This report, following soon after the work of Hermann[2] in the development of alternating positive and negative pressures for the treatment of the same type of disease, has further stimulated interest in the whole subject of therapy for vascular disorders. Thrombophlebitis, however, apparently has been excluded from consideration. We are unaware of any report of the effect of either intermittent venous occlusion or alternation of positive and negative pressures in the treatment of this condition. Indeed, the great majority of the advocates of both the above mentioned types of treatment have felt that the presence of thrombophlebitis constituted one of the contraindications to their use. The apparent reason for this is the fear that any increase in the venous pressure or mechanical massage of the affected extremity might increase the likelihood of the occurrence of pulmonary embolism. As far as is known there is no direct experimental or clinical evidence to support such a fear, at least as regards the intermittent venous occlusion treatment of Collens and Wilensky.[1]

Most of the problems inherent in the treatment of thrombophlebitis remain unsolved. In recent years the belief that cases of acute thrombophlebitis either occurring postoperatively or otherwise should not be subjected to too long a period of immobilization has been fairly generally accepted and probably with considerable improvement in the end results. Nevertheless convalescence is prolonged and the occurrence of the disabling sequelae of pain and chronic lymphedema appear frequently enough to merit the reporting of any new method of treatment which offers hope of still further improving the results in this condition.

TECHNIQUE EMPLOYED

Four cases of thrombophlebitis of the lower extremities of recent origin and seven cases with a duration of two months or longer have

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been treated with intermittent venous occlusion at the University of Minnesota Hospitals. The immediate results in this small series of unselected cases have been so striking that, despite the lack of adequate controls and follow-up study, they merit an early report. At the present time it must be admitted that no satisfactory rational explanation for the results obtained can be given. Certain experimental studies planned for the future should throw light on this subject.

After establishing a diagnosis of thrombophlebitis on the basis of history and physical examination, patients have been treated continuously for three to four hours a day five to six days a week with intermittent venous occlusion. During each period of treatment, patients were kept recumbent with the lower extremities slightly elevated. Venous occlusion was produced by wrapping a rubber bag 6 inches wide and 24 inches long around the midthigh and holding it in place with a loosely applied elastic bandage. This bag was then inflated with air to 70 to 80 mm. Hg for two minutes. This period of inflation was followed by a period of deflation of equal length during which a slight negative pressure was maintained within the rubber bag. Thus, a four-minute cycle was used. These pressure and time relationships probably fall within the optimal range for the production of reactive hyperemia. Several types of apparatus, such as that described by Collens and Wilensky,[1] now can be purchased which will produce satisfactorily the alternating inflation and deflation automatically. A similar type of apparatus has been employed in the cases reported.

No other form of treatment has been employed in any of the reported cases. In three instances (Cases 1, 2, and 3) treatment was carried out with the patients hospitalized and in bed. The other eight cases have been ambulatory.

CASE SUMMARIES

Acute Thrombophlebitis.—

CASE 1.—Mrs. O. C., University Hospital No. 670867. A very obese, 40-year-old housewife was operated upon Oct. 3, 1938, for the removal of a large apron of fat on the anterior abdominal wall. The operative wound became infected and an atelectasis of the right lung developed. These complications had practically subsided when on Oct. 18 a sudden sharp pain occurred in the right chest. A diagnosis of pulmonary infarction was made. On Oct. 20 pain and swelling of the right leg with tenderness along the course of the femoral vessels were noted. Eight days later a similar condition was noted in the left leg. Both legs were placed in casts and elevated.

There had been a septic febrile temperature throughout the convalescence. This persisted with the development of the thrombophlebitis despite the fact that the wound infection had cleared up and the chest was normal to physical examination.

On Nov. 9, 1938, thirty-eight days after operation, treatment by means of intermittent venous occlusion of both legs was instituted. A total of 15.5 hours of

treatment was given during the course of four days. Fig. 1 shows the effect of treatment upon the pulse and temperature. The pain and tenderness in the legs subsided promptly with the fever. On the other hand, the edema, which at no time was more than moderate in amount, subsided somewhat more gradually. At the time of discharge from the hospital on Nov. 20 there was no edema of the legs when the patient was up out of bed for short intervals. The patient was last seen on Dec. 20, 1938. At that time the only residual from the thrombophlebitis was slight swelling of the ankles if the patient was up and about for several hours.

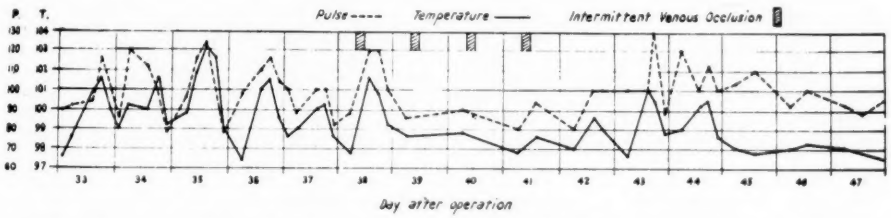
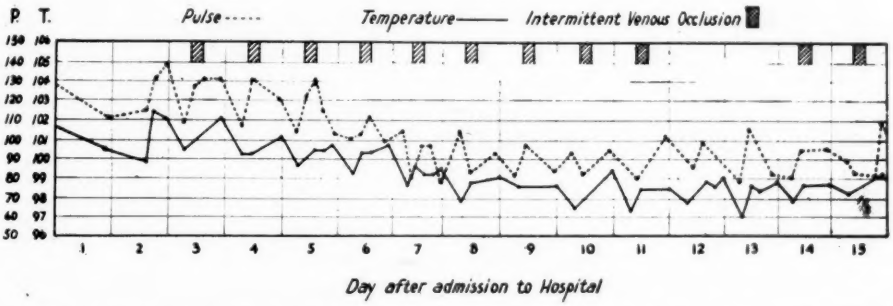


Fig. 1.—A portion of pulse and temperature chart of Mrs. O. C. (University Hospital No. 670876). This patient had acute thrombophlebitis of both legs five weeks after abdominal lipectomy. The effect of intermittent venous occlusion on the pulse and temperature is striking.

Case 2.—Mr. M. D., University Hospital No. 647385. A 21-year-old farmer had his left lower leg removed Nov. 9, 1938, for a myxofibrosarcoma of the foot. A moderate postoperative reaction subsided by the third postoperative day. On Nov. 17 the patient's temperature rose to 99.6°. On the following day the temperature was 100.4° and the patient complained of pain and tenderness along the course of the femoral vessels in the stump of the left leg. By Nov. 22 the temperature had returned to normal, but the pain and tenderness remained. On Nov. 23 intermittent venous occlusion was begun. After five days, a total of 15 hours of treatment, there had been no return of the fever and all pain and tenderness had disappeared. A slight degree of edema which was noted before treatment was begun appeared to be unchanged.



,Fig. 2.—A portion of the pulse and temperature chart of Mrs. M. S. (University Hospital No. 651847). This patient had a mild acute thrombophlebitis of the left leg twelve days after delivery of a premature infant. The effect of intermittent venous occlusion is much less striking in this case than in the case of Mrs. O. C., shown in Fig. 1.

Case 3.—Mrs. M. S., University Hospital No. 651847. A 32-year-old housewife was admitted to the hospital and delivered of a premature infant Nov. 14, 1938. On Nov. 26, after being out of bed for the first time, the patient noted pain in the medial portion of her left thigh extending from the groin down into the calf of her leg. The following day the entire left leg was swollen and painful. These symptoms and findings, combined with a daily rise of temperature to 100 to 101°

F., persisted until Dec. 1 when intermittent venous occlusion was begun. Treatments were given daily up to Dec. 30, 1938, a total of 81 hours.

After each period of treatment for the first three days this patient complained of an increased amount of pain. The pain and tenderness together with the fever then promptly disappeared and did not return. The edema of the limb remained the same despite the long period of treatment. The patient was discharged from the hospital Dec. 30, 1938, and has not been seen since.

CASE 4.—Mr. A. St. A., University Hospital No. 674405. A 56-year-old nightwatchman in November, 1938, while convalescing in another hospital after an attack of coronary thrombosis, fell to the floor and bruised his right lower leg. During the succeeding two days the right lower leg became tender, swollen, and warmer than the opposite leg. These symptoms subsided within two weeks and the patient was discharged from the hospital. A week later a recurrence of these symptoms occurred. When this patient was first seen on Nov. 30, 1938, the right lower leg was swollen with an indurated edema. The muscles of the calf were tender to pressure. Over the thigh distended superficial veins could be seen. The entire extremity was warmer to the touch than the opposite.

Intermittent venous occlusion was begun on Dec. 2, 1938, and continued to Jan. 5, 1939. A total of 84 hours of treatment was given. No appreciable improvement was noted until after 26.5 hours of treatment had been given. The patient then noted that within the space of two days the pain, which had been present continually to some degree and in an increased amount when he walked, suddenly disappeared. After approximately 60 hours of treatment, the patient stated that his leg felt perfectly normal. The edema had decreased to the extent that the soft tissues of the lower leg became more pliable. The size of the affected leg, however, appeared to be unchanged. An additional 24 hours of treatment were given at the patient's own request.

Chronic Thrombophlebitis.—

CASE 5.—Mr. W. A., University Hospital No. 642535. A 73-year-old retired farmer noted the sudden onset of dull pain in the left leg and thigh in July, 1938. Within 24 hours a similar pain was noted in the opposite leg and both lower extremities became swollen. Several weeks of rest in bed with the application of massive hot packs failed to relieve the condition.

When the patient was seen on Oct. 11, 1938, physical examination showed that both lower extremities were swollen with pitting edema. This edema was more indurated and of greater degree below the knees than above. Tenderness was minimal. There was no cyanosis of the feet or legs.

On Oct. 11, 1938, intermittent venous occlusion was begun in both legs for three to four hours a day and continued to Nov. 12. A total of 89 hours of treatment was given. After 12 hours of treatment, the patient stated that the pain in his legs had disappeared. After 40 hours of treatment, it was noted that the edema of the legs was less, the tissues were more pliable, and subjectively the legs were less stiff. This improvement continued during the remainder of the course of treatment. At the time of writing this patient has not returned for further observation.

CASE 6.—Mrs. M. McN., University Hospital No. 622335. A 64-year-old housewife with hypertensive heart disease was operated upon Aug. 5, 1938, for a recurrent nodular goiter with hyperthyroidism. Convalescence after a subtotal resection of the thyroid gland was uneventful until the day of her discharge when a feeling of fullness over the anterior medial aspect of the right thigh was noted shortly after leaving the hospital. Three hours later the leg pained quite severely and had begun to swell. On the following day she re-entered the hospital. Treat-

ment of the affected leg by elevation and heat relieved some of the swelling, but not the pain.

When this patient was seen on Oct. 14, 1938, she complained of persistence of the pain in the right leg which was greatly aggravated by walking. There was slight edema of the right ankle and lower leg as well as a subjective sensation of stiffness. The left lower extremity appeared normal.

Intermittent venous occlusion was begun on Oct. 17, 1938, and continued to Nov. 3. It was commenced again on Dec. 12 and discontinued on Dec. 23, a total of 88.5 hours. After 20 hours of treatment, marked subjective improvement was noted. Walking became easier, the stiffness of the joints was less pronounced, and the tissues about the right ankle were less indurated. At the end of the course of treatment, the patient could walk indefinitely without any difficulty and the slight edema noted at first had disappeared.

CASE 7.—Mr. D. S., University Hospital No. 673317. A 46-year-old farmer had influenza followed by thrombophlebitis of both legs in 1918. Massive edema of both lower extremities and extending up to the inguinal ligaments associated with local cyanosis and distended superficial veins ensued and persisted for twenty years. A continuous dull pain aggravated by walking or standing also developed.

When this patient was first seen on Oct. 28, 1938, many large tortuous superficial veins were present over the lower abdomen. The lower extremities from Poupart's ligament down to the dorsum of the feet were greatly swollen. The lower legs and feet were purplish blue in color and continually wet with perspiration. Many varicose veins were seen over both legs.

Intermittent venous occlusion was begun on both legs Oct. 29 and continued to Nov. 22, a total of 58.5 hours. After 15.5 hours of treatment, the patient remarked that his legs felt much better as far as the persistent pain was concerned. According to several observers, the edema had decreased a great deal. It is to be regretted that neither a photograph nor measurements of the legs were taken before treatment was begun. On Nov. 18, 1938, the edema had further decreased though the feet and lower legs remained cyanotic. At this time the patient stated that for the first time in twenty years he could cross his knees. Measurements of the circumference of the legs at this time were as follows:

	RIGHT LEG	LEFT LEG
Ankle	24.0 cm.	24.0 cm.
Calf	36.0 cm.	34.0 cm.
Lower thigh	48.0 cm.	44.0 cm.
Upper thigh	57.0 cm.	55.5 cm.

After 13 hours' more treatment and then seventeen days without treatment and without the support of elastic bandages, the legs were remeasured at the same levels as before:

	RIGHT LEG	LEFT LEG
Ankle	24.5 cm.	23.5 cm.
Calf	36.0 cm.	33.5 cm.
Lower thigh	43.5 cm.	42.0 cm.
Upper thigh	54.0 cm.	53.0 cm.

On Dec. 28, 1938, the patient died from a massive gastric hemorrhage. Postmortem examination revealed a large gastric ulcer with an eroded artery in its base. The inferior vena cava and both common iliac veins were occluded by an old canalized thrombus.

CASE 8.—Mr. M. R., University Hospital No. 673806. A 33-year-old foundry worker noted the onset of a painless swelling of the left lower leg in August, 1938. Five weeks in bed with leg elevated and the application of hot packs caused the

swelling largely to disappear. When the patient got up, however, the leg became painful and the swelling promptly returned and gradually progressed up the leg so that by October the lower portion of the thigh was swollen and by November the whole lower extremity below the inguinal ligament was involved. Pain was present throughout the leg on exercise and a certain stiffness of all the joints was present.

Fig. 3.—Mr. M. R. (University Hospital No. 673806). *A*, Indurated edema of the left leg before treatment by intermittent venous occlusion is marked; *B*, after 85.5 hours of treatment, the edema of the left leg is greatly reduced; this patient was ambulant throughout the whole course of treatment except during the periods of intermittent venous occlusion.

When the patient was first seen on Nov. 15, 1938, the right leg appeared normal. There was pitting edema of the entire left leg and thigh with areas of induration around the ankle. Measurements of the circumference of the leg were as follows:

	RIGHT LEG	LEFT LEG
Ankle	21.0 cm.	28.5 cm.
Calf	36.0 cm.	45.0 cm.
Lower thigh	40.0 cm.	48.0 cm.
Upper thigh	49.5 cm.	55.5 cm.

Intermittent venous occlusion was begun Nov. 15, 1938, and continued to Dec. 13, 1938, 85.5 hours being given. This patient noted no improvement during the first 24 hours of treatment, but then noted that the pain in his leg, which was increased when he walked, gradually disappeared. Soon thereafter the foot and ankle began to lose their stiffness. On Dec. 1, 1938, the edema of the foot and ankle had decreased to such an extent that the patient could put his shoe on for the first time in over three months. Improvement continued slowly from this time on to Dec. 13 when treatment was stopped. On this date measurements of the circumference of the leg at the same places as before were as follows:

	RIGHT LEG	LEFT LEG
Ankle	20.0 cm.	24.0 cm.
Calf	35.0 cm.	42.0 cm.
Lower thigh	38.5 cm.	48.0 cm.
Upper thigh	50.0 cm.	55.5 cm.

On Dec. 14, 1938, the patient went hunting and walked for seven hours. There was no recurrence of the pain in the leg, but when next seen on Dec. 16 the circumference of the legs was as follows:

	RIGHT LEG	LEFT LEG
Ankle	21.0 cm.	27.0 cm.
Calf	36.0 cm.	45.0 cm.
Lower thigh	39.0 cm.	48.0 cm.
Upper thigh	51.0 cm.	55.5 cm.

When the patient was last seen on Jan. 6, 1939, there had been no further change in the size of the leg. The patient felt no discomfort or stiffness, however, if he was on his feet for as long as ten hours at a time.

Fig. 2 shows the change in appearance of the leg before and after treatment.

CASE 9.—Mrs. E. L., University Hospital No. 673974. A 38-year-old housewife had a spontaneous abortion in April, 1938. Three weeks later, pain and tenderness along the course of both femoral veins and a diffuse swelling of both legs up to the groin appeared. The usual treatment of elevation of the legs and application of heat was instituted and persisted in for several weeks. No improvement occurred except some decrease in the amount of swelling. Pain, severe enough to keep the patient confined to her bed at home, persisted up to Nov. 16, 1938, when she was admitted to the hospital.

Examination at that time showed the skin of both lower extremities to be dry and scaly. A moderate pitting edema was present in both legs. Along the course of the femoral vessels and over both calves there was extreme tenderness to pressure.

On Nov. 17, 1938, intermittent venous occlusion was started on both legs and repeated daily until Dec. 1 when a total of 38.5 hours had been given. No appreciable change occurred in the amount of edema, but there was a complete relief of the pain. When discharged from the hospital on Dec. 2, 1938, she could be up for short periods without increase in the edema or recurrence of the pain.

CASE 10.—Mr. E. G., University Hospital No. 673389. A 60-year-old laborer who weighed 277 pounds and had hypertension and auricular fibrillation began to limp with the left leg in August, 1938. This leg soon thereafter became swollen and painful, especially when he walked. Rest in bed for seven weeks failed to improve the condition. During this time reddish colored spots which were tender to touch appeared over the calf. These areas would disappear after a few days, only to reappear in a new location.

When this patient was first seen on Nov. 18, 1938, there were no signs of cardiac decompensation. The left leg and thigh were markedly swollen from the level of the inguinal ligament downward. The foot and ankle were cyanotic and the skin over them tense and shiny. The calf of the lower leg and the medial and lateral aspects of the thigh were tender to firm pressure.

Intermittent venous occlusion was started Nov. 21, 1938, and continued daily until Dec. 2, 1938. The patient stated that after the first day's treatment (3.5 hours) his leg felt more limber. On Dec. 2, after 37.5 hours' treatment, he said that the pain in his thigh and leg had disappeared. Tenderness on pressure over the calf and thigh was no longer present. The edema, however, appeared to be unaffected.

CASE 11.—Mr. J. McA., University Hospital No. 661140. A 69-year-old retired farmer while walking to his barn on Oct. 1, 1938, noted the onset of dull burning pain throughout the whole left thigh. Within twenty-four hours the entire left lower extremity became swollen and the superficial veins more prominent than on the opposite leg.

When seen on Dec. 2, 1938, the lower leg was markedly swollen with edema. The foot was bluish in color. All the superficial veins were distended. The patient's chief complaints were a constant dull pain throughout both the left thigh and left lower leg. In addition, there was stiffness in the left foot and ankle.

Intermittent venous occlusion was begun on Dec. 5, 1938, and continued daily until Dec. 23, when 58.5 hours had been given. There was no decrease in the edema as indicated by measuring the circumference of the leg. The skin and subcutaneous tissue about the ankle became less indurated, however. The pain and stiffness complained of before treatment was started were no longer present when treatment was discontinued.

RESULTS OF TREATMENT

In Table I the results of the treatment of the eleven reported cases of thrombophlebitis of the lower extremities by intermittent venous occlusion are summarized.

It will be noted that in each of the reported cases the pain, discomfort, and tenderness present in the affected extremity when intermittent venous occlusion was begun were relieved during the course of treatment. In some instances this occurred after only a few hours of treatment, but in certain cases twenty or more hours were required to accomplish the same result. The effect of intermittent venous occlusion on the edema present and its secondary effects, such as induration and stiffness of joints, was variable and unpredictable. The edema in certain cases was unquestionably decreased a great deal, in others improved somewhat, and in still others unaffected. If improvement did occur, a certain sequel of events characteristically occurred. Induration, if present, decreased first. The skin and subcutaneous tissues became softer and more pliable. The subjective stiffness of the joints improved as the induration decreased. In certain cases improvement in the edema progressed no further than this, no actual decrease in the size of the leg being demonstrable.

There has been an opportunity to observe the effect of the treatment on fever due to acute thrombophlebitis in two cases. Fig. 1 shows the course of the pulse and temperature before, during and after a short course of treatment in the case of Mrs. O. C. (University Hospital No. 670867). In the case of Mrs. M. S. (University Hospital No. 651847), Fig. 2, a more gradual subsidence of fever and elevated pulse occurred over three days' time.

DISCUSSION

It is fully realized that further studies, more inclusive and better controlled, will have to be made before the full significance of the results reported in this paper can be evaluated correctly. It is our

TABLE I

	DIAGNOSIS	DURATION OF SYMPTOMS WHEN TREATMENT BEGUN	TOTAL HOURS OF TREATMENT	EFFECT OF TREATMENT ON:			
				TENDERNESS, PAIN AND DISCOMFORT	SIZE OF LEG	INDURATION OF EDEMATOUS AREAS	STIFFNESS OF JOINTS
Case 1, Mrs. O. C. (U. H. No. 670867)	Acute thrombophlebitis, both legs	19 days	15½ hr.	Relieved	Decreased	*	*
Case 2, Mr. M. D. (U. H. No. 647385)	Acute thrombophlebitis, left leg	5 days	15 hr.	Relieved	No change	*	*
Case 3, Mrs. M. S. (U. H. No. 651847)	Acute thrombophlebitis, left leg	5 days	81 hr.	Relieved	No change	*	*
Case 4, Mr. A. St. A. (U. H. No. 674405)	Acute thrombophlebitis, right leg	3 wk.	84 hr.	Relieved	No change	Decreased	*
Case 11, Mr. J. Mc.A. (U. H. No. 661140)	Chronic thrombophlebitis, left leg	2 mo.	58½ hr.	Relieved	No change	Decreased	Relieved
Case 6, Mrs. M. Mc. N. (U. H. No. 622335)	Chronic thrombophlebitis, right leg	2 mo.	88½ hr.	Relieved	Decreased	Decreased	Relieved
Case 10, Mr. E. G. (U. H. No. 673389)	Chronic thrombophlebitis, left leg	3 mo.	37½ hr.	Relieved	No change	*	Relieved
Case 5, Mr. W. A. (U. H. No. 642535)	Chronic thrombophlebitis, both legs	3 mo.	89 hr.	Relieved	Decreased	Decreased	Relieved
Case 8, Mr. M. R. (U. H. No. 673806)	Chronic thrombophlebitis, left leg	3 mo.	85½ hr.	Relieved	Decreased	Decreased	Relieved
Case 9, Mrs. E. L. (U. H. No. 673974)	Chronic thrombophlebitis, both legs	6½ mo.	38½ hr.	Relieved	No change	*	No change
Case 7, Mr. D. S. (U. H. No. 673317)	Chronic thrombophlebitis, both legs	20 yr.	38½ hr.	Relieved	Decreased	Decreased	Relieved

*These conditions were not present.

firm conviction, however, that intermittent venous occlusion in some way favorably influences the subjective symptoms and the disturbed circulation of limbs in which acute or chronic thrombophlebitis exists.

Very little is known concerning the pathologic physiology of thrombophlebitis. If three questions could be answered, the rational approach to an effective therapy would be placed on a much sounder basis. These questions are: What is the nature of the inflammatory process in the affected veins? What are the causes of the pain? What produces the edema?

Considerable confusion exists in the minds of clinicians as to the distinction which should be made between the pathologic process known as thrombosis and the clinical process known as thrombophlebitis. The histologic picture of an old thrombus may be indistinguishable from that of an old thrombophlebitis, yet the one may have given no clinical symptoms and the other may have given all the signs of an acute local inflammation. The study of thrombophlebitis from the viewpoint of bacteriology has been sadly neglected. The authors are unaware of any worthwhile investigation as to the incidence of bacteria in the thrombi of thrombophlebitis. The impression is gained, however, that in many cases the inflammatory process of thrombophlebitis develops, runs its course, and subsides in the absence of bacterial infection. Further investigations should be carried out to clarify this aspect of the problem.

Leriche[5] recently has set forth the idea that the pain associated with acute thrombophlebitis may be due to an associated spasm of blood vessels, both veins and arteries, in the affected limb. To relieve this vascular spasm he has in some instances infiltrated the lumbar sympathetic ganglia with novocain and in other cases removed these ganglia surgically. Such procedures have relieved much if not all of the pain in certain cases of both acute and chronic thrombophlebitis studied by Leriche. Ochsner[6] in 1938 reported satisfactory results in patients treated in this manner.

The importance of the venous obstruction present in thrombophlebitis in the production and maintenance of the edema is debatable. Experimentally it has been shown that simple ligation of the principal veins in an extremity will not produce a permanent edema. Homans[3] has further shown that in many cases of phlegmasia alba dolens there is an associated perivenous inflammation and infiltration of the perivenous tissue with a plastic exudate. He has stated that in these cases the persisting edema may be explained by a block of the trunk lymphatics which course through this inflammatory tissue. The experimental production of lymphedema in the hind legs of dogs by the injection of sclerosing substances into the trunk lymphatics reported by Homans, Drinker, and Field[4] lends substantial support to this idea. While such an explanation seems quite adequate in certain cases where

the existence of inflammation as judged by clinical signs seems incontrovertible, other writers, and even Homans himself, have been reluctant to explain the edema in all cases of thrombophlebitis on this basis.

The work of dos Santos[7] in the delineation of the extent of the venous occlusion by roentgenologic examination after the injection of radio-opaque solutions into the peripheral veins offers a new approach to the subject of thrombophlebitis. He himself feels that this method offers a safe, early method of diagnosis, localizes the thrombus, offers a differential diagnosis of edemas and acute affections of the limbs, and gives evidence of the presence or absence of venous spasm. The exact interpretation of the roentgenograms obtained by dos Santos' technique is not easy. If the occlusion of the veins shown in some of his films is due to the presence of thrombi within them, the thrombotic process is much more extensive than is usually thought. It may be, however, that some portion of this occlusion is due to compression of the veins by the pressure of the edema in the surrounding tissues or to spasm of the smooth muscle in the walls of the veins.

On the basis of our present knowledge, the benefits from intermittent venous occlusion exhibited by the patients reported in this paper cannot be fully explained. It is well recognized that the occlusion of veins of an extremity will increase the venous pressure at points distal to the site of occlusion. Furthermore, increased venous pressure is always followed by increased flow of lymph. When venous occlusion is intermittent, however, another factor comes into consideration; namely, reactive hyperemia. None of these effects without further investigation can be asserted to be the effectual agent in our treatment of thrombophlebitis. It may be possible that the increased venous pressure due to occlusion dilates veins more or less occluded by extrinsic pressure, or that an increased flow of lymph dilates in a similar fashion compressed lymph channels. If Leriche is correct in his idea that pain in thrombophlebitis is due to vascular spasm, it may well be that the effects of reactive hyperemia relieve this spasm equally as well as interruption of the sympathetic nerve fibers does.

These various possibilities only emphasize the need of fundamental physiologic investigation of the disturbed vascular and lymphatic systems in thrombophlebitis. We propose to study additional cases by making venograms after the technique of dos Santos before and after treatment. In addition, changes in venous pressure and tissue tension are to be noted. It will have to be determined if an occluding pressure of 70 to 80 mm. Hg and a 4-minute cycle are within the optimal range for this condition. In the experimental laboratory the effect of intermittent external compression of the thigh of the dog on total blood flow, arterial pressure, and venous pressure, in the deep as well as superficial veins, will be studied.

A few clinical measurements already have been made. The venous pressures in the superficial veins of the lower leg during the course of distention and deflation of the occluding cuff have been measured in two cases. These measurements show that when the occluding cuff is distended to 70 to 72 mm. Hg (95 to 98 cm. H_2O) the pressure in the superficial veins distal to the point of occlusion rises to 75 to 76 cm. H_2O and remains at this level until deflation occurs at the end of the 2-minute period. During the 2-minute period in which the cuff is deflated, the venous pressure falls to 10 to 13 cm. of water.

Comparable results have been obtained in similar studies on two dogs. Rubber cuffs were wrapped loosely around the thighs and the changes in venous pressure in the femoral vein proximal to the cuff and in the external saphenous vein distal to the cuff have been followed as the cuff was distended to various pressures. These pressure variations are given in Table II.

TABLE II

	PRESSURE IN OCCLUDING CUFF	PRESSURE IN VEIN	PRESSURE IN FEMORAL VEIN
Dog 1	0 mm. Hg	23.5 cm. H_2O	3.5 cm. H_2O
	120 mm. Hg	79.0 cm. H_2O	10.0 cm. H_2O
	100 mm. Hg	75.5 cm. H_2O	
	80 mm. Hg	53.5 cm. H_2O	
	60 mm. Hg	42.5 cm. H_2O	
	40 mm. Hg	28.0 cm. H_2O	
	20 mm. Hg	18.0 cm. H_2O	
	10 mm. Hg	17.0 cm. H_2O	
	0 mm. Hg	21.0 cm. H_2O	5.0 cm. H_2O
Dog 2	0 mm. Hg	12.0 cm. H_2O	3.5 cm. H_2O
	100 mm. Hg	104.0 cm. H_2O	1.5 cm. H_2O
	80 mm. Hg	81.0 cm. H_2O	
	50 mm. Hg	66.0 cm. H_2O	
	40 mm. Hg	51.5 cm. H_2O	
	30 mm. Hg	42.0 cm. H_2O	
	10 mm. Hg	25.5 cm. H_2O	
	0 mm. Hg	12.0 cm. H_2O	4.0 cm. H_2O

These few simple observations indicate the most obvious physiologic change produced by intermittent venous occlusion, but they explain not at all the reason for improvement in clinical cases. They lend support rather to the criticism which can be raised against this form of treatment; namely, that such a procedure may increase the likelihood of pulmonary infarction of embolism. Whether or not this is so cannot be settled by rationalization. In the eleven cases we have treated thus far, no signs of embolism have occurred.

SUMMARY

Four cases of acute thrombophlebitis and seven cases of chronic thrombophlebitis of the lower extremities have been treated with intermittent venous occlusion. A rubber cuff 24 inches long and 6 inches wide was applied to the midportion of the thigh and intermit-

tently inflated to a pressure of 70 to 80 mm. Hg. A 4-minute cycle was used with two minutes of inflation and 2 minutes of deflation, continued for three to four hours a day. Pain, tenderness, and discomfort were relieved in each case. In some instances the edema was decreased. In two patients the venous pressure distal to the point of occlusion was measured to be 75 to 76 cm. H_2O in the period of inflation and 10 to 13 cm. H_2O in the period of deflation. Comparable venous pressure changes in normal dogs have been observed when a pressure cuff was applied to their thighs and distended.

Certain problems bearing on the treatment of thrombophlebitis which should be elucidated have been discussed.

CONCLUSIONS

1. Treatment of patients with acute and chronic thrombophlebitis of the lower extremities by means of intermittent venous occlusion relieved the pain, tenderness, and discomfort in eleven unselected cases. In some cases edema was decreased.

2. The distention of a rubber bag applied to the midthigh of patients with thrombophlebitis increases the pressure in the superficial veins of the lower leg to 75 to 76 cm. H_2O if the bag is distended to 70 to 72 mm. Hg for 2 minutes. If the cuff is then deflated, the venous pressure falls to normal levels.

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THE EFFECT OF INTRAVENOUS HYPERTONIC SUGAR SOLUTIONS ON TRAUMATIZED TISSUES*

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THE intravenous administration of hypertonic solutions has been widely used clinically, especially in head injuries. So far as can be ascertained from the literature, this procedure is based on studies of the dehydrating effect of intravenous hypertonic solutions on normal tissues and no investigation of the results of intravenous hypertonic solutions on traumatized edematous tissues has been found.

METHODS

Two tissues of healthy young male rabbits were subjected to trauma. In the first group trauma to one ear was produced by hitting with a felt-padded reflex hammer for a period of five minutes. The other ear was not traumatized in order to offer comparable normal tissues. In the second group the triceps and gastrocnemius muscles on one side were similarly traumatized under intraperitoneal sodium ethyl barbiturate anesthesia, the contralateral muscles not being traumatized for comparison. After a lapse of twenty-four hours, during which the animals were allowed food and water, control animals were sacrificed by a blow upon the occiput and the remaining animals were injected in the femoral vein with 8 c.c. per kg. of a 50 per cent solution of either sucrose or glucose. The solutions were freshly made and injected at body temperature at the rate of 5 c.c. per minute. The experimental animals were sacrificed at various intervals up to two hours after injection, being allowed no intake of water or food during the experimental period. The ears were amputated close to the head and the muscles were dissected and excised. Tissues were discarded if there was gross hemorrhage. Surplus blood was sponged away from the tissues with gauze. Fat was extracted from the minced muscle with ether. The wet weights of all the tissues were obtained and the tissues were dried to a constant weight in an oven at 105° C. and reweighed.

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RESULTS

Ears, 50 Per Cent Sucrose Injections (Table I).—The values for the average percentage of water in the normal and traumatized ears dropped comparably at 30 minutes after injection. At 60 minutes after injection, the value for the normal ear remained unchanged, but that for the traumatized ear rose slightly above the preinjection level. At 120 minutes, the values in both instances were lower than the preinjection levels but higher than the values at the 30-minute, postinjection period. The maximum decreases in tissue fluid were less than twice the standard errors of the differences and are therefore without statistical significance.

TABLE I*

FLUID CONTENT (PER CENT OF WET WEIGHT) OF NORMAL AND TRAUMATIZED RABBIT EARS AT VARIOUS INTERVALS AFTER INTRAVENOUS INJECTION OF 50% SUCROSE, 8 C.C. PER KG. OF BODY WEIGHT

EAR		SUCROSE 50%			
		CONTROL	PERIODS AFTER INJECTION		
			30 MIN.	60 MIN.	120 MIN.
		PER CENT	PER CENT	PER CENT	PER CENT
Normal	Min.	67.1	67.0	64.1	66.4
	Max.	73.5	71.2	72.7	72.5
	Ave.	70.7 ± 0.44 (18)	69.1 ± 0.77 (6)	69.1 ± 1.6 (6)	69.4 ± 0.42 (18)
Traumatized	Min.	68.3	71.8	66.2	67.4
	Max.	85.8	76.7	82.7	82.3
	Ave.	75.8 ± 1.05 (18)	74.1 ± 0.81 (6)	76.1 ± 3.15 (6)	74.6 ± 1.12 (18)

*The figures in parentheses indicate the number of individual observations from which the averages were obtained. The apparent decreases in fluid content of both normal and traumatized ears at all intervals after injection are not significant as compared with the control levels.

Muscle, 50 Per Cent Sucrose and 50 Per Cent Glucose Injections (Tables II and III).—The changes in the average percentage of water in the normal and traumatized muscles roughly paralleled each other at the 5-, 15-, 30-, 60-, and 120-minute intervals after injection. The lowest water content of the muscle occurred 15 minutes after sucrose injection and 5 minutes after glucose injection. At these intervals the actual decreases were more than the standard errors of the differences and the results are therefore significant.

DISCUSSION

It should be noted that the range between individual minimum and maximum values of tissue water in the controls is greater, even in the normal tissues, than the difference between the control average and the lowest average after injection. This comparison is exaggerated in the traumatized group as the result of obvious difficulty in the standardization of the amount of trauma. The fact that any dehydrating effect had been obtained therefore might be questioned were it not for the constancy with which injection was followed by a slight

TABLE II*

FLUID CONTENT (PER CENT OF WET WEIGHT) OF NORMAL AND TRAUMATIZED RABBIT MUSCLES AT VARIOUS INTERVALS AFTER INTRAVENOUS INJECTION OF 50% SUCROSE, 8 C.C. PER KG. BODY WEIGHT

MUSCLE		SUCROSE 50%					
			PERIODS AFTER INJECTION				
		CONTROL	5 MIN.	15 MIN.	30 MIN.	60 MIN.	120 MIN.
		PER CENT	PER CENT	PER CENT	PER CENT	PER CENT	PER CENT
Normal	Min.	77.5	76.5	76.1	76.2	76.6	77.1
	Max.	80.1	77.5	77.6	79.1	78.2	80.6
	Ave.	78.6 ± 0.24 (12)	77.1 ± 0.14 (12) S	76.7 ± 0.18 (12) S	77.2 ± 0.27 (12) S	77.3 ± 0.18 (12) S	78.2 ± 0.29 (12)
Traumatized	Min.	77.4	76.1	76.3	76.9	77.0	77.4
	Max.	83.9	80.9	79.9	82.2	82.4	81.4
	Ave.	80.1 ± 0.60 (12)	78.5 ± 0.47 (12) S	78.0 ± 0.32 (12) S	79.1 ± 0.50 (12)	79.4 ± 0.62 (12)	79.4 ± 0.38 (12)

*The figures in parentheses indicate the number of individual observations from which the averages were obtained. The letter S signifies a statistically significant difference between the average value immediately above and the corresponding control.

TABLE III*

FLUID CONTENT (PER CENT OF WET WEIGHT) OF NORMAL AND TRAUMATIZED RABBIT MUSCLES AT VARIOUS INTERVALS AFTER INTRAVENOUS INJECTION OF 50% GLUCOSE, 8 C.C. PER KG. BODY WEIGHT

MUSCLE	GLUCOSE 50%					
			PERIODS AFTER INJECTION			
		CONTROL	5 MIN.	15 MIN.	30 MIN.	60 MIN.	120 MIN.
		PER CENT	PER CENT	PER CENT	PER CENT	PER CENT	PER CENT
Normal	Min.	77.5	74.6	76.0	75.5	76.5	76.7
	Max.	80.1	77.3	78.8	77.3	79.1	77.7
	Ave.	78.6 ± 0.24 (12)	76.1 ± 0.27 (12) S	77.1 ± 0.29 (12) S	76.2 ± 0.17 (12) S	77.7 ± 0.26 (12) S	77.1 ± 0.12 (12) S
Traumatized	Min.	77.4	75.5	77.0	78.2	76.9	78.0
	Max.	83.9	80.5	80.7	81.4	81.6	81.6
	Ave.	80.1 ± 0.60 (12)	77.9 ± 0.47 (12) S	78.9 ± 0.40 (12)	79.7 ± 0.33 (12)	79.8 ± 0.50 (12)	79.9 ± 0.39 (12)

*The figures in parentheses indicate the number of individual observations from which the averages were obtained. The letter S signifies a statistically significant difference between the average value immediately above and the corresponding control.

decrease in water content of the tissues and for the statistical validity of the values for muscle. The apparent absolute dehydrating effect is a maximum in all tissues studied of only 2.5 per cent of wet weight.

Parallelism between the dehydration curves of normal and traumatized tissues is almost complete. It therefore appears that intravenous hypertonic sugar solutions in heavy dosage produce water withdrawal from normal or traumatized rabbit ears and muscles to so slight an extent as to be of no practical importance.

CONCLUSIONS

1. Withdrawal of water from the normal ear and muscle of the rabbit following the intravenous injection of hypertonic sugar solutions is slight and reaches its maximum within thirty minutes.

2. Dehydration of traumatized edematous tissues by the same means is parallel to that of normal tissues.

THE TREATMENT OF ACUTE (NONTUBERCULOUS) EMPYEMA BY IRRIGATION AND NEGATIVE TENSION

Preliminary Report

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MANY methods have been advocated in the management of the acute (nontuberculous) empyemas between the time Hippocrates[1] suggested watchful waiting and that of drainage with contralateral pneumothorax recently suggested by Koster and his co-workers.[2] As early as 1889 Storch[3] advocated water suction aspiration in the treatment of empyemas. In 1898 Perthes[4] devised a negative tension apparatus for the evacuation of pus from the pleural cavity; in 1920 Moschowitz[5] showed that the maintenance of a negative tension in the pleural cavity helped evacuate the pus, and in 1934 Wangensteen[6] rediscovered the value of negative intrapleural tension in the treatment of empyema.

When we examine the results of all methods suggested for the treatment of empyemas and their modifications, we note that the mortality rate in the more commonly employed methods is more or less the same. Assuming therefore that therapy is instituted at the optimum time, if one seeks to reduce the mortality, he has but little choice between the various methods. However, in these same statistical reports we note that there is a wide difference in the morbidity. In the method which we are about to describe we have been able to reduce the morbidity at the Kings County Hospital from an average of 53 days of postoperative hospitalization to 37.3 days. In those cases in which negative tension drainage was employed all patients remained in the hospital until the sinus was healed and roentgenographic examination of the chest showed persistent clearing of the pleural cavity and complete expansion of the lung. Before this method was introduced, many of the patients who were treated by the conventional methods of intercostal drainage or rib resection drainage, were discharged with residual pneumothoraces or unhealed sinuses. So that, the postoperative period of hospitalization in the latter group of cases would be even greater had we subjected them to the same rigorous criteria as the cases we are reporting in this communication.

The proposed method is cognizant of the contributions of MacCallum[7] on the pathology of empyema, of Graham and Bell[8] on the relation of open pneumothorax to the treatment of empyema, and the work of

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Aufrect[9] on the relation of the size of thoracotomy to the rate of the lung expansion. Regardless of the method employed, cure of any acute (nontuberculous) empyema requires (1) the evacuation of the pus at the optimum time, (2) the sterilization of the pleural cavity, (3) the complete expansion of the lung, and (4) the restitution to integrity of the thoracic cage. The present method does not present anything radically new in the treatment of empyema but rather emphasizes the principles governing the management of empyema based upon the pathologic process within the pleural cavity and, second, some advantages which may be obtained in the maintenance of a normal negative intrapleural tension. The acute nontuberculous empyemas may be subdivided into six groups; namely, (1) pneumococcic, (2) streptococcic, (3) pneumococcic and streptococcic, (4) staphylococcic, (5) anaerobic or facultative anaerobic, and (6) any combination of the foregoing. The latter three groups are distinct entities requiring special treatment not afforded by this method nor by the usual methods employed in the treatment of empyema, and are therefore omitted. The proposed method is particularly applicable to infections of the pleural cavity which are secondary to the usual pneumonias, pneumococcic and streptococcic.

Pneumococcic empyema is generally secondary to a pneumococcic pneumonia and is postpneumonic. Early in the course of the disease, the pus tends to become thick and is accompanied by a semiorganized fibrinous coagulum. The pus is relatively thick from the outset but tends to become thicker during the first two weeks. At the same time the coagulum becomes more organized. To attempt an early cure of such an empyema by means of simple aspiration or by means of an intercostal drainage must of necessity be doomed to failure more often than success. There is no doubt, however, that such empyemas have been cured by these methods, only at the expense of a prolonged morbidity. Those who have recognized the shortcomings of the above methods have suggested the use of the wide caliber tubes for drainage, with or without irrigation. Drainage under such conditions is more adequate, but not infrequently the tube becomes obstructed by the coagulum and the drainage impeded. If still larger tubes are used, i.e., one which will permit the coagulum to pass readily, it will also permit air to enter the pleural cavity at the same rate as it enters the trachea and therefore will inhibit the expansion of the lung. Such interferences with adequate drainage and expansion of the lung are obviated in the method about to be described, and in our cases have given satisfactory results.

METHOD

The patient is anesthetized in the usual manner. We prefer local paravertebral block anesthesia in the adult and general anesthesia in

the infant. The patient is postured either before the local anesthesia or after the general anesthesia, as the case may be, so that he rests on the contralateral side with the arm on the affected side drawn across the anterior chest. A rib is selected in the axillary region (usually the eighth rib), the interspace above which is the lowest point through which pus can be aspirated. About one and one-half inches are resected subperiosteally. This exposes the parietal pleura. A wet towel is then placed about the walls of the wound, leaving a small central area through which the pleura can be seen. A knife is then passed through the exposed pleura, and, as it is withdrawn, the towel is compressed. This prevents the flow of the pus into the wound. The pressure is gradually released and a suction tip is passed into the pleural cavity through the opening. As much of the pus is evacuated as is possible. The towel is then removed. The pleura is opened from one end of the cut rib to the other, leaving the suction tip in place. The pleural cavity is now aspirated under direct vision, removing the residual pus and coagulum. The larger pieces of coagulum may be removed with a dressing forceps. The pleural cavity is then flushed with warm normal saline solution and again aspirated. This irrigation and aspiration is continued until all the coagulum and pus are removed and the underlying lung shows signs of expansion. It is imperative that all the coagulum be removed. A soft rubber tube about one-half inch in diameter is prepared so that it contains a one-inch collar drawn to about one and one-half inches from the tip. This tube is then placed into the pleural cavity so that the tip points backwards and downwards towards the diaphragm. The pleura is then closed tightly about the tube with several interrupted black silk sutures. The intercostal muscles are approximated with interrupted chromic catgut sutures. The muscle sutures nearest the tube are so placed that they include the collar on the tube. This fixes the tube in place. The skin is then closed with interrupted black silk sutures and again the sutures nearest the tube are placed so that they include the collar. The pleural cavity is then filled with warm normal saline solution (through the tube), after which the tube is clamped with a hemostat. A collodion or rubber cement soaked gauze dressing or liquid adhesive is then applied to the skin over the wound and about the tube at the site of its entrance into the thorax. When dry this forms an airtight dressing. The patient is then returned to his bed and placed in the semi-orthopnoeic position as soon as feasible. The drainage tube is then connected to a glass Y-tube, the upper arm of which is attached to a suspended irrigating container and the lower arm to a glass subaqueous drainage tube, Fig. 1. The subaqueous tube rests on the bottom of a colorless glass bottle and about four inches below the surface of water in the bottle. This collecting bottle should be placed below the level of the bed, preferably on the floor at the patient's bedside. A

screw stopcock is then placed on the tube leading from the chest, proximal to the hemostat, closed tightly, and the hemostat removed. The irrigating bottle is filled with normal saline solution. When all the air in the system has been expelled, the rubber tube leading to the irrigating container is clamped with the hemostat, Fig. 1*A*. During the first three or four hours postoperatively the stopcock should be opened gradually, allowing a slow trickle of the pleural content. In about three hours the stopcock should be completely opened allowing a free communication between the pleural cavity and collecting bottle. In about six or eight hours the flow will stop spontaneously. At this time the stopcock may be removed. It will be noted that the respiratory excursions of the thorax are accompanied by fluctuations in the glass drainage tube. Thus, the intrapleural pressure will be expressed in the fluctuations within this tube. When the stopcock is first opened, the intrapleural pressure being positive, there will be no fluid level within this tube. As the pleural cavity rids itself of its contents, the intrapleural pressure becomes negative and the fluid level in the tube rises in response to the negative pressure within the pleural cavity. This pressure becomes increasingly negative until an equilibrium is established. The maximum negative pressure is reached usually within about twelve hours.

Irrigation of the pleural cavity is begun about eight hours postoperatively. The substance of the instructions to the patient or nurse is as follows:

The hemostat on the irrigating tube (Fig. 1*A*) is removed and placed on the drainage tube (Fig. 1*B*). This allows the irrigating solution to flow into the pleural cavity. The patient allows the fluid to enter the cavity until he feels a tightness in the chest. The hemostat is then replaced in its original position—Fig. 1*A*. This allows the pleural content to drain out into the collecting bottle. When the flow has ceased, the patient is turned toward the affected side and encouraged to cough. This helps expel the residual fluid. The irrigation is repeated every two or three hours.

After twenty-four hours of the above procedure, the tube originally inserted into the thorax is clamped proximal to the Y-tube and the connections thereto removed. A mercury manometer is connected to the upper arm of the Y-tube, and the negative pressure apparatus, shown in Fig. 2, is connected to the lower arm of the Y-tube. A Murphy drip tube is then placed in the siphon drainage system. A siphon drainage is established from Bottle 2 to the collecting bottle. The stopcock at *C* in Fig. 2 is then closed so as to allow only a slow drip through the Murphy tube. This creates a negative pressure which is transmitted to the pleural cavity and registered in the manometer. The siphonage should be so regulated that the intrapleural pressure approximates that within the normal pleural cavity.

With the patient in the semiorthopnoeic position, the pressure should be about –10 mm. of mercury at the end of normal inspiration and –5 mm. of mercury at the end of normal expiration. Once the desired pressure is reached it can be maintained by the slow drip of the siphonage at about five drops per minute, after which the apparatus works automatically. When Bottle 2 becomes empty, the tubing proximal to the Y-tube is clamped with a hemostat and filled with colored water. The siphonage is then reestablished and the pressure noted. When the manometric reading is the same as that before the tube was clamped off, the hemostat is removed. This least disturbs

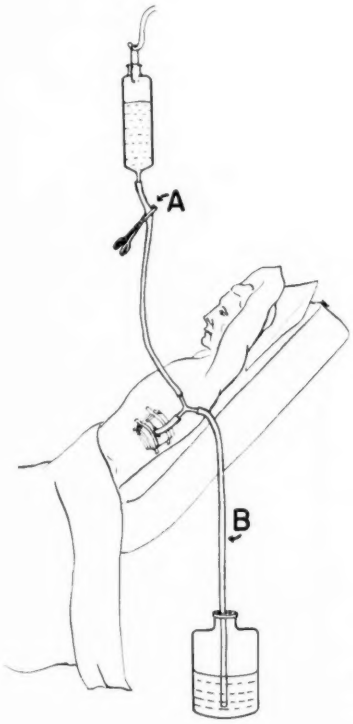

Fig. 1.

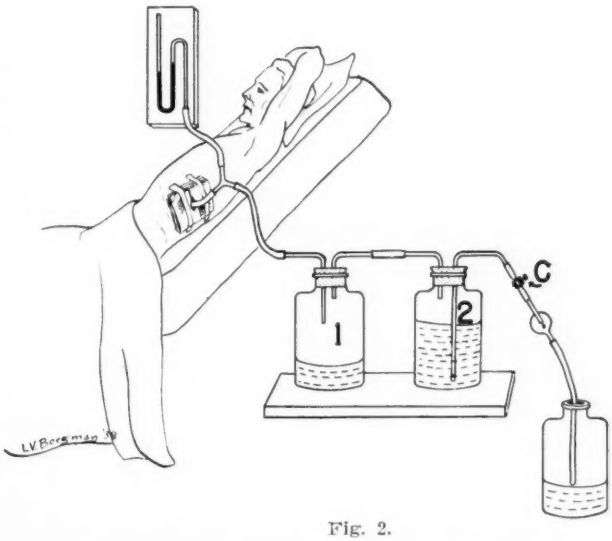

Fig. 2.

Fig. 1.—Shows the method of attaching the irrigating container and collecting bottle to the tube in the chest. The hemostat in position *A* prevents the fluid from entering the pleural cavity, but permits the pleural content to pass into the collecting bottle. When the hemostat is placed in position *B*, the irrigating fluid enters the pleural cavity.

Fig. 2.—Shows the attachment of the manometer and simple aspiration (siphonage) system. The stopcock at *C* is used to regulate the siphonage and negative tension.

the equilibrium of the system. In about a week or ten days the lung should be completely expanded. A roentgenographic examination of the chest should be made at this time. The indications for the removal of the tube from the chest are (1) an afebrile state, (2) complete expansion of the lung, and (3) a minimum of retained fluid. Occasionally, however, a small area of incompletely expanded lung may be seen in the region of the tube and/or a small amount of fluid below

the level of the tube. These are no contraindications to the removal of the tube. A strip of rubber tissue is then placed into the sinus to prevent too rapid healing of the wound and at the same time to permit drainage of any residual fluid. The opening in the chest wall is cleansed and a dry dressing is applied to it. This wound usually heals within a week or ten days.

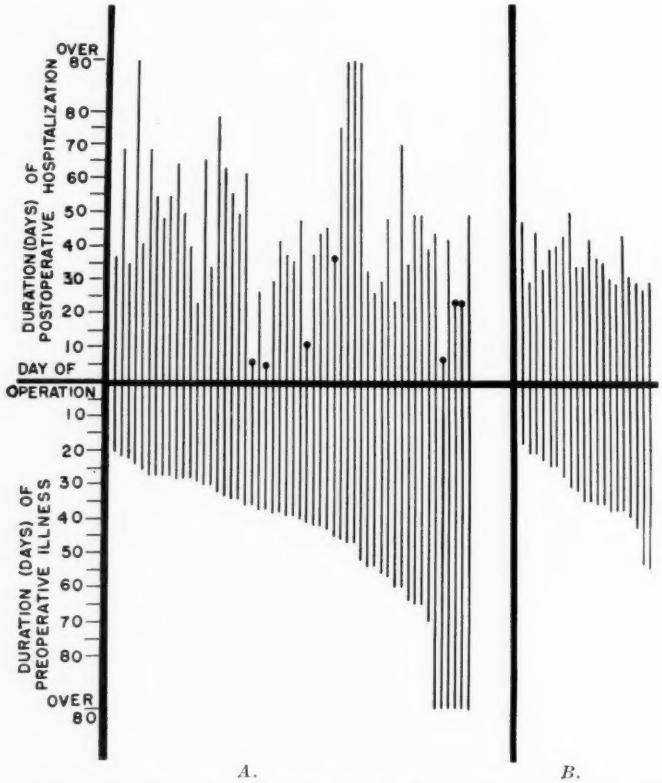

Fig. 3.—Shows the preoperative duration of the patients' illness and the postoperative period of hospitalization. Each vertical line denotes one case. This solid dot denotes a fatality and the postoperative day on which the patient succumbed. *A* denotes 53 unselected cases treated by methods other than negative tension. *B* denotes 20 unselected cases treated by irrigation and negative tension.

Streptococcic empyema is usually secondary to a streptococcic bronchopneumonia and occurs during the course of the latter disease. It is synpneumonic. The pus is relatively thin in the early course of the disease and is accompanied by a minimum of fibrinous coagulum. In the earliest stages of this disease repeated aspirations to relieve dyspnea, toxemia, or cardiac embarrassment may save the life of the patient. It is generally agreed that an empyema is not an emergent surgical condition. This is particularly true of the streptococcic empyemas. When the acute phase of the underlying disease has subsided, then the empyema may be considered as a surgical problem. The pus being thin and unaccompanied by fibrinous material, it is unnecessary, in most

cases, to evacuate the pleural contents through a large opening such as is obtained following rib resection. Secondly, the lung being nonadherent until rather late in the course of the disease the admission of air into the pleural space will increase the collapse of the lung and thereby increase the anoxemia. In streptococcic empyema a closed intercostal drainage will often suffice. The previously described slow subaqueous drainage, followed by irrigation and negative pressure aspiration, is applicable, as in the pneumococcic empyema cases. In the later stages of streptococcic empyema, i.e., those in which the pus has become thick, the procedure outlined for the pneumococcic empyemas may be followed.

We have compared the results of this method of treatment in 20 unselected cases of empyema with 53 unselected cases treated by rib resection or intercostal drainage without negative tension. The results are given in Table I. It will be noted that in those cases treated by irrigation and negative tension the postoperative period of hospitalization was 37.3 days; whereas, in the 53 cases treated by rib resection or intercostal drainage the time required was 47 days. In this latter group of cases there were 7 fatalities and therefore the average period of the postoperative hospitalization in the surviving 46 cases was 53 days. Examination of Fig. 2 shows that there were 39 cases treated by the usual methods in which the duration of the preoperative illness was the same as in the 20 cases treated by irrigation and negative tension. In this group of cases there were 4 fatalities. The postoperative period of hospital stay in the surviving 35 cases was 54 days. So that, regardless of how we compare the results, the morbidity is appreciably less in those cases treated by the method described.

COMMENT

No hard and fast rules can be formulated for any surgical procedure, especially in the treatment of empyema. All cases must be individualized; some will require longer subaqueous drainage (as the earlier streptococcic cases), others longer periods of irrigation (as in subacute or mixed empyemas), and still others will require longer periods of negative pressure aspiration (as in those instances in which there is thickening of the visceral pleura). In general, however, the above time is adequate for all cases. The one rule which may be considered as fixed is that whenever the patient becomes dyspneic or coughs a good deal or the negative pressure becomes too high, the tube just outside of the chest wall should be clamped for a few hours. At no time, however, have we had any such untoward symptoms. When they did occur, they were transitory and did not embarrass the patient's respiration.

TABLE I

A REVIEW OF 73 UNSELECTED SURGICAL CASES OF ACUTE (NONTUBERCULOUS) EMPYEMA, 20 OF WHICH WERE TREATED BY IRRIGATION AND NEGATIVE TENSION

Total number of cases	73
Number of cases treated by negative tension	20
Number of cases treated by other methods	53
Total number of deaths	7 (9.6%)
Total mortality in cases treated by negative tension	0 (0.0%)
Total mortality in cases treated by other methods	7 (13.2%)
Average number of postoperative days in hospital for the 73 cases	44.3
Average number of postoperative days in hospital for the 53 cases	47.0
Average number of postoperative days in hospital for the 53 cases minus the 7 fatal cases (46 cases)	53.0
Average number of postoperative days in hospital for the 20 cases treated by negative tension	37.3
Average number of postoperative days in the cases treated by other methods in which there was a similar length of preoperative illness (39 cases), minus the 4 fatalities, or 35 cases	54.0

Finally, we may add that in the pneumococcic cases the temperature usually drops to normal within the first three days after surgical intervention. In the streptococcic cases it may take a day or two longer. The lung is usually completely expanded within ten days after surgical intervention. An x-ray examination of the chest should be made at this time before the tube is removed. If no contraindications exist, the tube may be removed.

At the present time we feel encouraged by our results of irrigation at the time of surgical intervention and the maintenance of postoperative negative tension in the treatment of the acute nontuberculous empyemas.

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THE SPECIFIC GRAVITY OF THE PUS IN EMPYEMA

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WHEN should a thoracic empyema be drained? The answer to this question is important for it may influence the convalescence or even the life of the patient. That open operation done too early may be fatal was strikingly demonstrated in the postinfluenzal empyemas where the mortality dropped from 40 per cent to 4 per cent with delay in open drainage.[7] Graham and Bell[4] showed that many of these deaths were due to shifting of the mediastinum, diminished capacity of the contralateral lung, and asphyxia. If the patient survived this, a total pyopneumothorax often developed. Heuer,[6] Wangensteen,[9] Carlson,[2] Graham and Berck,[5] and in fact most authors in recent years have warned against premature open drainage in empyema. It has been generally accepted that time should be allowed for stabilization of the mediastinum and fixation of the lung before operation is performed. Conversely, undue delay is to be avoided for it permits thickening of the pleura and chronic empyema. Thus drainage at the optimum time will avoid fatal asphyxia, pyopneumothorax, or chronic empyema and promote rapid healing. The problem is to know what is the optimum time for drainage.

Most surgeons decide when to operate upon a patient with empyema by observing the course and duration of the disease and the character of the pus. They wait until the pus is "thick" or "creamy" or "will just pour" and infer from this that the process is localized to a walled-off abscess. This is ordinarily a safe method but since so much depends upon the change in the exudate it would appear desirable to judge it in a quantitative rather than a descriptive way. As pus thickens, the specific gravity should increase, so it was decided to measure this to see if it gave an estimate of the condition. Readings were obtained in 36 cases, of which 18 were due to the pneumococcus, 12 to the hemolytic streptococcus, 5 to *Staphylococcus aureus*, and 1 to the tubercle bacillus.

The cases of pneumococcus empyema showed a steady increase in the specific gravity of the pus during the first three weeks of the disease. The following readings were representative of average results: 7 days, specific gravity 1015; 9 days, specific gravity 1017; 14 days, specific gravity 1025; 15 days, specific gravity 1027; 18 days, specific gravity 1034; 21 days, specific gravity 1040.

It was noted that in about three weeks after onset the specific gravity of the pus reached 1040. It leveled off here and did not go higher no

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matter how long the process existed. Some patients were operated upon without any difficulty before this level was reached. Whether or not this will always be true can only be determined by greater experience.

The pus in cases of staphylococcus empyema was much like that from the pneumococcus infections. In contrast to these the exudate in *Streptococcus haemolyticus* empyema had a lower specific gravity at a comparable time in the disease. Fig. 1 shows typical examples of this condition. Here it is seen that a slow steady elevation of the specific gravity occurs, with ultimate fixation at a constant level. When this stage is reached, open drainage of the chest should be a safe procedure.

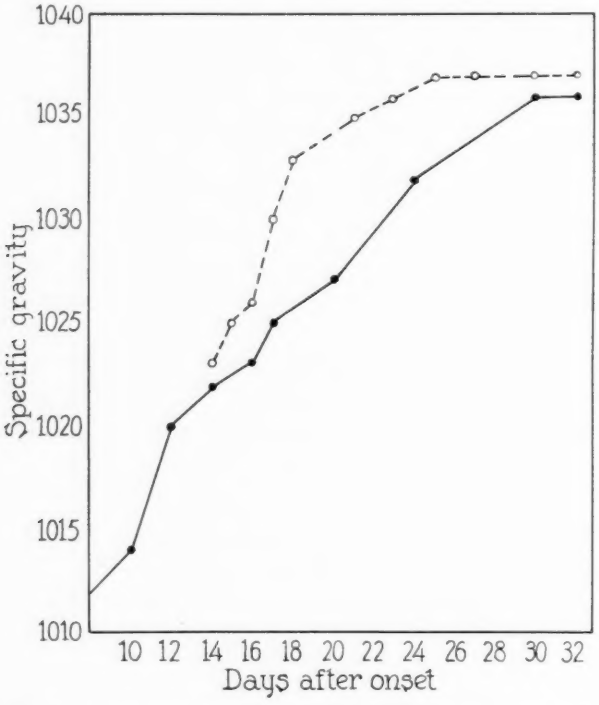

Fig. 1.—The rise in the specific gravity of the pus in two cases of streptococcus empyema. Note the tendency to establish a constant level at about four weeks after the onset of the disease.

DISCUSSION

Direct efforts have been made to determine a safe time for open drainage of empyema. Berman[1] observed cases under the fluoroscope and found that in normal individuals or in those with early empyema the mediastinum changed in width with respiration, being wide with expiration and narrow with inspiration. He stated that when the mediastinum ceased to move with respiration, then localization had occurred, so operation was safe. Yet apparently this only indicates fixation and stiffening of the mediastinum and does not show that the lung is attached to the chest wall. Until this attachment occurs, open operation may allow collapse of the lung with resultant pyopneumothorax.

Fraser[3] uses the level of intrathoracic pressure to determine the stage of an empyema. He states that the normal negative pressure becomes plus-minus with pleural effusion and positive with a localized abscess. The accumulation of pus in a walled-off infection creates a positive pressure. No mention of the use of this method was found in the literature, but it would appear to be valuable.

The study of the character of the pus is an indirect method of estimating the stage of the infection. It is simple and has been widely used. The measurement of the specific gravity of the exudate gives a quantitative expression to this estimate which makes for greater exactness. Other physical changes in the pus also may be indicative of the stage of the disease, so data are now being obtained on the viscosity, cell count, and hematocrit. Such information, if correlated with the clinical signs, should assist in an accurate estimation of the condition. It may tell us exactly when a thoracic empyema should be drained.

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LYMPHOPATHIA VENEREA AND THE FREI TEST*

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SINCE the advent of the Frei Test in 1925 as a specific means of diagnosing lymphopathia venerea, the literature has been flooded with articles concerning this disease. With the possible exception of carcinoma, there perhaps has been as much or more written on this subject in the last ten years as upon any other subject. Yet, despite such enthusiasm, there is an apparent feeling in some localities that lymphopathia venerea is still a rare disease. Or, on the other hand, there is a tendency to believe that it has become a "wastepaper basket" term, a name to be given to any lesion occurring about the genitals or rectum which presents no apparent etiology. That certain disease processes which are labeled lymphopathia venerea do exist is willingly admitted. But, there is an unwillingness to diagnose them as such, simply on the basis of the positive Frei test, although one may find some forty or fifty references in the literature favoring the specificity of this test.

Therefore, it was the purpose of this study to add further evidence as to just how specific the Frei test is, particularly in the study of certain genital and rectal conditions as seen in the colored race.

The patients studied were mainly those seen routinely in the Proctologic Outpatient Department of Baylor University Hospital, Dallas, Tex. All patients, irrespective of their complaints, were subjected to Frei tests. About sixteen different Frei antigens were used, with the thought in mind that patients might vary in their reactions, or that certain antigens might be more potent than others. The average variety of antigens given any one patient was 4.7; the most to any patient was 10. In many instances the patient was given repeated tests with the same antigen, it being felt that, in order to consider one as definitely having lymphopathia venerea, there should be a positive reaction either with most of the antigens used or a consistently positive response with the same antigen. Therefore, the greatest number of tests given any one patient was 15, the average per patient being 6.2. The total number of patients studied in this manner was 42.

Females	35
White	7
Colored	28
Males	7
White	0
Colored	7

*Thesis submitted to the faculty of the Graduate School of Medicine of the University of Pennsylvania in partial fulfilment of the requirements for the degree of Master of Medical Science (M.Sc. [Med.]) for graduate work in surgery.

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CLASSIFICATION OF THE SYMPTOMS OF LYMPHOPATHIA VENEREA

Lymphopathia venerea is a disease with many syndromes. Usually the clinical manifestations can be placed in one of four general groups: inguinal adenitis, genitoanal involvement, rectal stricture, and urethral involvement. Of course, there will be more or less overlapping of groups, depending on the extent of the infection in any one patient.

Fig. 1.—J. M., aged 32 years, colored male. There were some ten to twelve sinus tracts over the right buttock, which had been present for about six years. In addition, he had two more tracts opening upon the scrotum. No apparent connection with the rectum. Biopsy report: "Chronic inflammation of subcutaneous tissue with areas of focal necrosis. Etiology not apparent." Patient gave positive Frei reaction with three different antigens.

Inguinal Adenitis.—As has been so often described, this phase of lymphopathia venerea is seen most frequently in the male because of the difference of lymphatic drainage of the sexes. It is of interest to remember that as early as 1859 Chassaignac recognized this condition as a definite clinical entity, believed it to be of venereal origin, and gave a truly modern-day description of the involved lymph glands. It was, of course, Nicolas, Favre, and Durand, in 1913, who first be-

lieved the disease to be not only of venereal origin, but also an infection of the genital lymphatics as well.

Of the series of 42 cases studied, 5 were classed in this group (Table I).

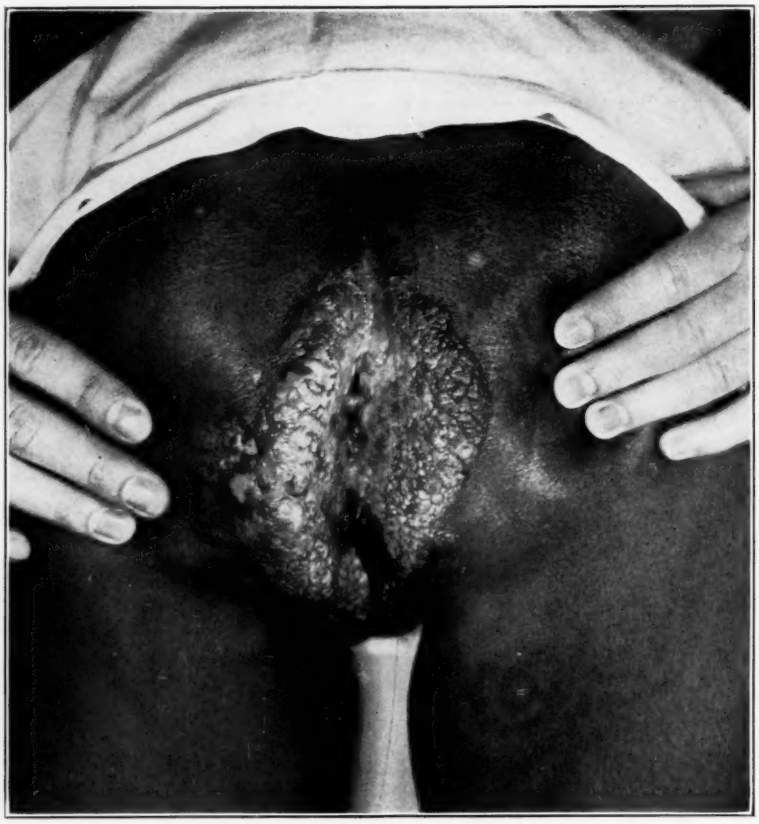

Fig. 2.—Q. S., aged 25 years, colored female. The granulomatous mass pictured about the rectum and vagina had been present for about eight years. Had been surgically removed once, but returned. She complained of "bloody pus" coming from the rectum. Had consistently negative Wassermann, Kline, and Kahn tests, and denied ever having received antisyphilitic treatment. Gave consistently positive reactions to three different Frei antigens. See Fig. 3 for biopsy report.

Genitoanal Syndrome.—This group includes a great variety of pathologic processes seen in lymphopathia venerea, most often in the female. Elephantiasis of the vulvae and chronic ulceration of the labia, perineal body, and anal region were described by Hugier in 1848, and the name of "anorectal syphiloma" applied by Fournier in 1875. In addition to the elephantiasis and the esthiomene of the vulvae, there may be all sorts of fistulas and sinuses about the vagina, anus, rectum, scrotum, and apparently even the buttocks (Fig. 1). Condyloma-like masses may occur about the vagina or rectum (Fig. 2). Many writers, in discussing rectal strictures, have described the presence of anal ulcers and fissures, anal fistulas, pruritus ani, hypertrophic anal tags, etc., as

a sort of prestenotic phase of stricture.[1, 19, 31] However, it would appear that many such conditions, particularly as seen in the negro, may be the result of infection with the virus of lymphopathia venerea and may be present without evidence of rectal stricture. Such opinion, however, depends upon acceptance of a positive Frei test in these cases as significant evidence of lymphopathia venerea.

Fig. 3.—Q. S. Biopsy report: "The section is cut in such a manner that the thickened epithelium with acanthosis shows cords extending through entire section. The spaces between these epithelial columns consist of loose, edematous fibrous tissue infiltrated with many plasma cells, a few eosinophiles, and lymphocytes. There are a few small areas of coagulation necrosis. The fibrous tissue is moderately vascular." Diagnosis: infectious granuloma of the skin with marked hyperplasia of the epithelium.

Of the series of 42 cases studied, it was found that 20 might be placed in the so-called genitoanal syndrome group (Table II).

Rectal Stricture.—There perhaps has been more written and more discussion about this phase of lymphopathia venerea than any other. It is of particular interest that, beginning with Copeland in the nine-

TABLE I

NAME	AGE	SEX	RACE	DURATION OF CONDITION	SEROLOGY
1. E. F.	24	F	C	1 mo.	negative
2. R. C.	21	F	C	1 mo.	positive
3. O. O.	20	M	C	1 mo.	negative
4. A. B.	23	M	C	1 mo.	positive
5. W. F.	49	M	C	2 mo.	negative

teenth century, when he believed rectal strictures were of venereal origin, the etiology of such has been blamed, almost chronologically, upon syphilis, tuberculosis, and gonorrhea. Since the origin of the Frei test, practically all clinics are reporting rectal strictures as 100 per cent the result of lymphopathia venerea. It is now well known that most rectal strictures occur in the female and predominantly in the colored race. In this respect it should be remembered that in 1923 Rosser[28] brought forth the term "fibroplastic diathesis" as descriptive of the negro's tendency to form excessive fibrous tissue following infection or irritation. (Fig. 4.) It cannot be doubted that this factor alone is responsible for the appearance in our clinics of a higher percentage of colored than white women with rectal strictures of lymphopathia venerea origin. However, Mathewson,[24] in a report from San Francisco, brings forth a significant point when he finds that of 78 patients with rectal stricture, 60 were men.

Sixteen of the 42 cases in this series had rectal stricture (Table III).

TABLE II

NAME	AGE	SEX	RACE	CONDITION PRESENT	DURATION	SEROLOGY
1. J. M.	27	F	C	Anal ulcer	18 mo.	Positive
2. L. M.	20	F	C	Anal fissure	3 mo.	Positive
3. E. C.	26	F	C	Infected anal keloid	9 mo.	Negative
4. E. R.	19	F	C	Anal condylomas	12 mo.	Negative
5. Q. S.	25	F	C	Anal condylomas	8 yr.	Negative
6. A. G.	32	F	C	Anal fistula		
				Anal ulcer	3 yr.	Positive
7. F. W.	31	F	C	Anal fistula		
				Anal ulcer	3 yr.	Negative
8. L. E.	20	F	C	Anal fistula	3 mo.	Positive
9. D. J.	24	F	C	Anal sinus	1 yr.	
10. M. B.	25	F	C	Esthiomene	4 yr.	Negative
11. E. A.	55	F	C	Pruritus ani	20 yr.	Negative
12. L. R.	27	F	C	Granular proctitis		Negative
13. G. S.	28	F	C	Anal ulcer		
				Vaginal ulcers	1 yr.	Negative
14. A. R.	39	F	W	Urethral stricture		
				Anal condylomas		
				Hypertrophic anal papillae	2 yr.	Negative
15. L. S.	37	F	W	Pruritus ani	2 yr.	Negative
16. P. D.	39	F	W	Pruritus ani	1 mo.	Negative
17. C. L.	27	M	C	Scrotal fistula	3 yr.	Positive
18. R. B.	28	M	C	Scrotal fistula	1 yr.	Negative
19. L. B.	36	M	C	Anal fistula	5 yr.	Negative
20. J. M.	32	M	C	Buttock sinuses		
				Scrotal fistula	6 yr.	Negative

TABLE III

NAME	AGE	SEX	RACE	DURATION OF STRICTURE	SEROLOGY
1. M. W.	28	F	C	2 yr.	Negative
2. C. S.	76	F	C	9 yr.	Negative
3. J. B.	39	F	C	8 yr.	Negative
4. B. H.	26	F	C	4 yr.	Positive
5. H. P.	32	F	C	5 yr.	Negative
6. B. T.	23	F	C	7 yr.	Negative
7. E. L.	27	F	C	9 yr.	Positive
8. M. S.	44	F	C	2 yr.	Negative
9. C. J.		F	C		
10. G. W.	33	F	C	1 yr.	Negative
11. M. H.	27	F	C	5 yr.	Negative
12. A. J.	23	F	C	4 yr.	Negative
13. J. A.	27	F	C	2 yr.	Negative
14. I. Q.		F	W (Mex.)		
15. R. L.	28	F	W	1 yr.	Negative
16. N. M.	64	F	W	8 yr.	Negative

Urethral Syndrome.—Little seems to have been mentioned in the literature as to this phase of lymphopathia venerea as a specific entity. Yet, it would appear to be almost as important as a clinical manifestation of lymphopathia venerea in the colored male as the rectal stricture is in the colored female. Martin[24] estimates that 92 per cent of urethral strictures as seen in the colored male are the result of this disease. Here again, however, one wonders what part is played by the fibroplastic diathesis as described by Rosser, and the fibroplastic tendencies in negro urethral disease as indicated by Day as early as 1921. Gray,[12] in 1936, described 25 cases of urethral involvement in the female, of which 23 gave positive Frei reactions. As stated by him: "The disease presents a syndrome—a chronic urethritis, with or without intra urethral ulceration, which may remain extremely chronic and indolent or may proceed to urethral stricture, or to ulcerative destruction of the urethra; the ulceration may extend beneath the clitoris and labia, or about the introitus and deeply to the sides of the rectum; elephantiasis vulvae may be associated." In the series of cases studied in this clinic, there has been one such patient whose condition seems worthy of brief description.

A colored female, 42 years of age, presented the symptoms of pain and straining with defecation, evacuation of blood and pus from the rectum, and continuous dribbling of urine, all over a period of four or five years. Examination of her genitorectal region revealed a chronic ulcerative process which had completely destroyed the urethra, the sphincter, and part of the trigone; there was a large opening between the vagina and rectum in the fore part of the vaginal vault; the rectum was stenosed and admitted only a small sound or rubber catheter. (Figs. 6 and 7.) Wassermann, Kline, and Kahn tests were negative. An x-ray of the chest showed chronically involved areas in the right chest, but repeated examinations of the sputum were negative. The patient gave positive tests with five different Frei antigens.

THE FREI TEST

In this study the Frei tests were given in the classical manner, 0.1 c.c. of the antigen being injected intradermally. In most instances the reaction was not read until the end of seven days, although it is generally accepted that seventy-two to ninety-six hours is the optimum time to read such. There were two reasons for establishing the seventh

Fig. 4.—C. S., aged 76 years, colored female. Was known to have had a rectal stricture ten years ago, but it is not known how long it existed before that. About eight years ago had a colostomy because of the obstructive nature of the stricture. Six months ago it was necessary to repeat the colostomy as shown here, because of the excessive keloid formation which had choked out the previous opening as seen below the present colostomy. It is this excessive overproduction of fibrous tissue that Rosser cells "fibroplastic diathesis" and which must play an important role in the formation of rectal stricture in the colored race. This patient failed to react to Frei tests.

day as the time of reading. Most of the patients were, as has been previously stated, those in the out-patient department, and it was soon learned that the majority of them would return to the clinic rather faithfully once a week, but that about one-half of them would fail to make an appearance if asked to come more often. Also, it was felt that even more accurate readings could be made at the end of seven

days, for if a positive reaction still existed at that time, it could be taken as a definitely positive Frei test and not a reaction of a non-specific protein type. Likewise, it was found that those Frei tests which were to be positive would still be quite positive on the seventh day.

Fig. 5.—J. B., aged 39 years, colored female. Gave a history of rectal stricture of eight years' duration. Of interest in this x-ray, aside from the very evident stricture, are the numerous sinuses and fistulous tracts surrounding the rectal and sigmoidal canals. Serology negative. X-ray of chest negative. Gave very definite positive Frei reactions to seven different antigens. (See Fig. 8.)

About sixteen different antigens were used. These antigens were of a variety of sources, some having been made in the usual way from the pus of the involved bubo. Others were from macerated inguinal glands, or macerated tissues from fistulous tracts, perineum, etc. Some of the antigens were of a 1:5 dilution, others 1:10, and several 1:20. A few were of the polyvalent type, being a mixture of several different antigens from respective patients.

The positive reactions obtained were generally one of four types: a small papule, a large papule, a pustule, or an ulceration (Figs. 8 and 9). No effort was made to measure the size of the papule. If a definite palpable nodule was still present at the end of a week, the Frei test was considered positive.

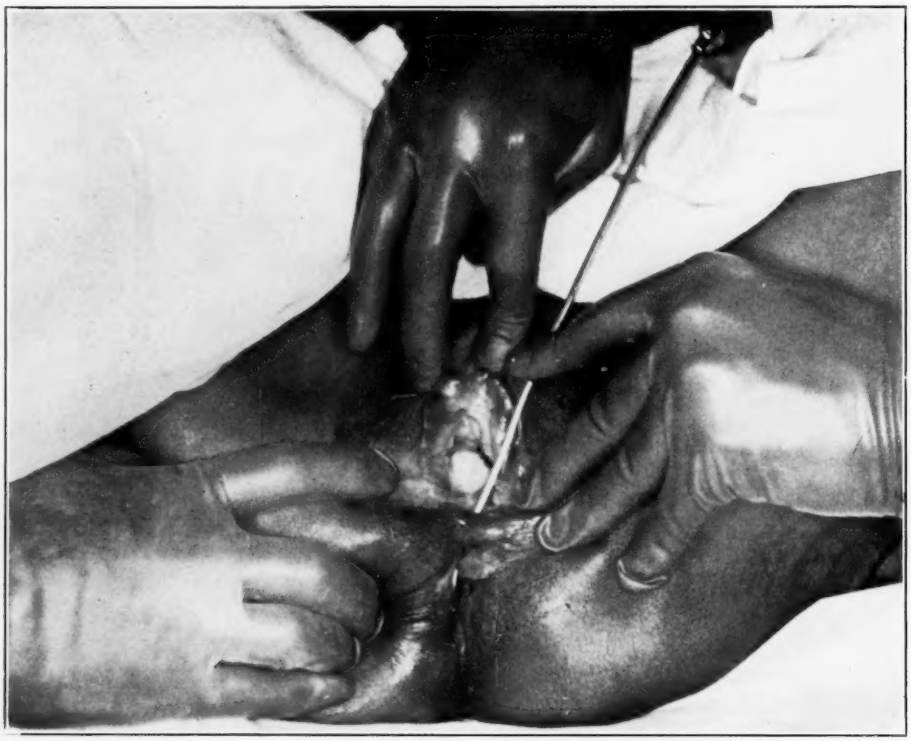

Fig. 6.—L. C., aged 42 years, colored female. In this illustration the cavity seen just below the clitoris is the bladder and shows to what extent the urethra has been entirely destroyed. The whitish mass just below this is the anterior portion of the upper vaginal wall. The vaginal canal is not seen here, but the mere slit pictured just below the protruding upper vaginal wall is the entrance to such. The probe is seen to pass through a wide opening in the anterior vagina to the anal canal. There is much scarring and contraction about the anus with stenosis of the anal and rectal canals. (See Fig. 7.) Frei positive with five different antigens.

Tables IV-VII illustrate better than a verbal description the specific manner in which each patient responded to each Frei test. Each "x" is a positive test, and each "–" a negative one. The initials of each patient are plotted against the number of the antigen of the sixteen antigens used in the study. The patients in the various groups are listed identically with the previous charts.

From a study of these tables, two facts are at once obvious. In the first place, it will be noted that of the entire group of 42 patients only 2 or 3 failed to give a positive Frei reaction with at least one antigen. Therefore, because of the many and varied factors involved in a correct interpretation of Frei tests, it was felt that only those patients who responded positively to 50 per cent or more of the antigens used

upon them, or, who gave repeatedly positive tests with the same antigen and were checked against control patients, should be considered as having lymphopathia venerea as indicated by their Frei tests. The following summary, therefore, is based upon such considerations:

Inguinal adenopathy group	60 per cent positive
Genitoanal group	80 per cent positive
Rectal stricture group	81 per cent positive
Urethral syndrome (1 case)	100 per cent positive
Total for the entire group	78 per cent positive

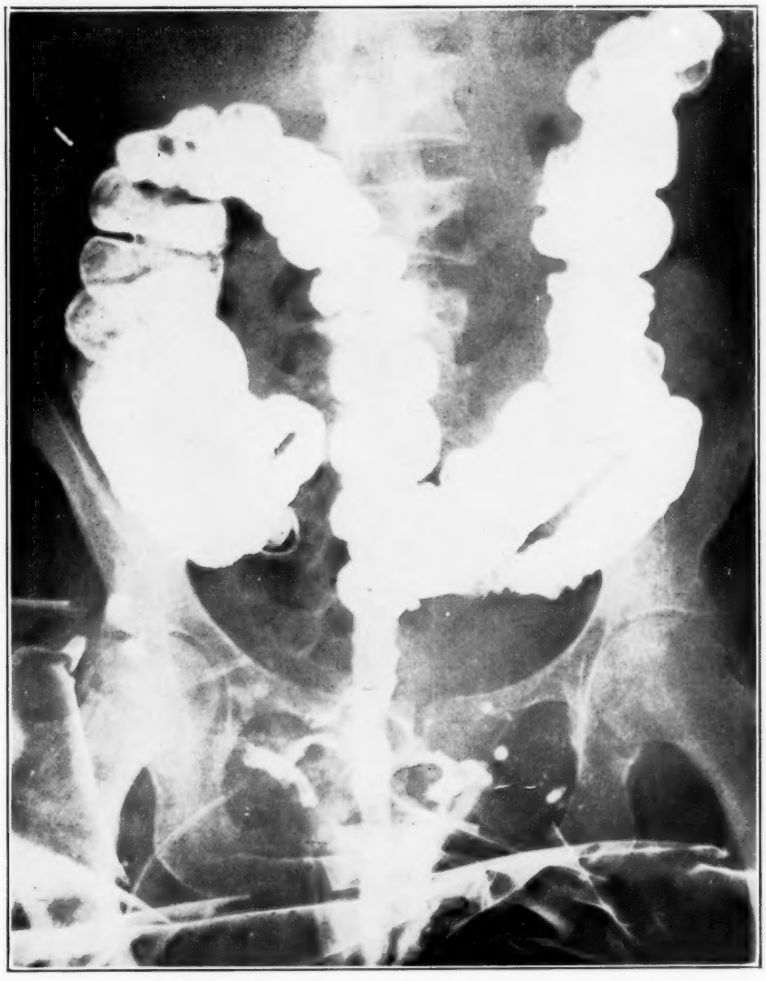

Fig. 7.—X-ray of case pictured in Fig. 6. This shows the strictured condition of the anal and rectal canals. Note again, as in Fig. 5, the large sinuses and fistulous tracts leading off the rectal canal.

The second fact noted about the foregoing tables is that certain antigens gave more positive reactions than others. This would appear to be the result of either a variation in the patient's susceptibility to a

given antigen, or a variation in the potency of different antigens. Coutts and Bianchi[8] have offered the explanation that such variations are due to subgroups of the virus responsible for lymphopathia venerea. Anderson and Harmos[2] found that antigens made from macerated inguinal glands were rather weak, and for the most part such has been

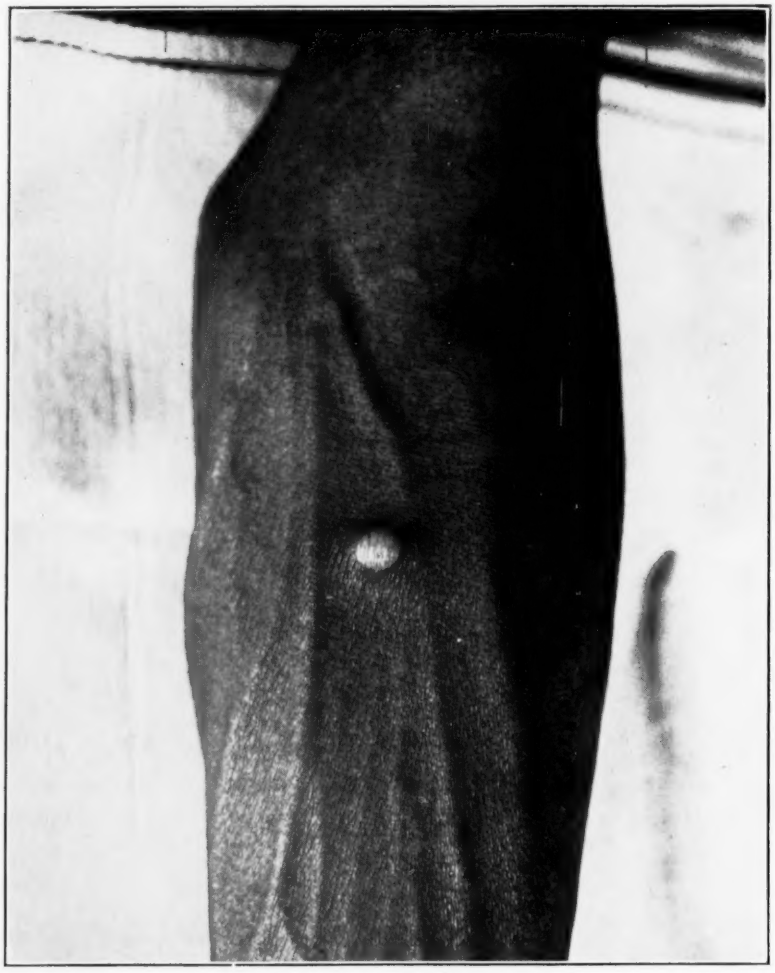

Fig. 8.—J. B. Same patient as shown in Fig. 5. Frei test as it appeared at the end of a week. She gave similar reactions to seven different antigens.

the experience of the author. Anderson and Harmos also report that the dilution of the antigen played very little part in the results obtained. Sullivan and Ecker[33] have stated that the present dosage of Frei antigen far exceeds the necessary amount. However, in this study there have been several patients who failed to give a positive Frei test, even with the more potent antigens, unless the dosage was increased. It has been said that the age of the antigen will vary the results obtained with it, that any antigen should not be used much

after six months from the time of its production. Several of the antigens used in this clinic have been three years old and yet have given good results. Such, of course, have been checked from time to time for evidence of bacterial contamination, and have been used upon other control patients.

Table VIII illustrates the variations of the antigens used in this clinic.

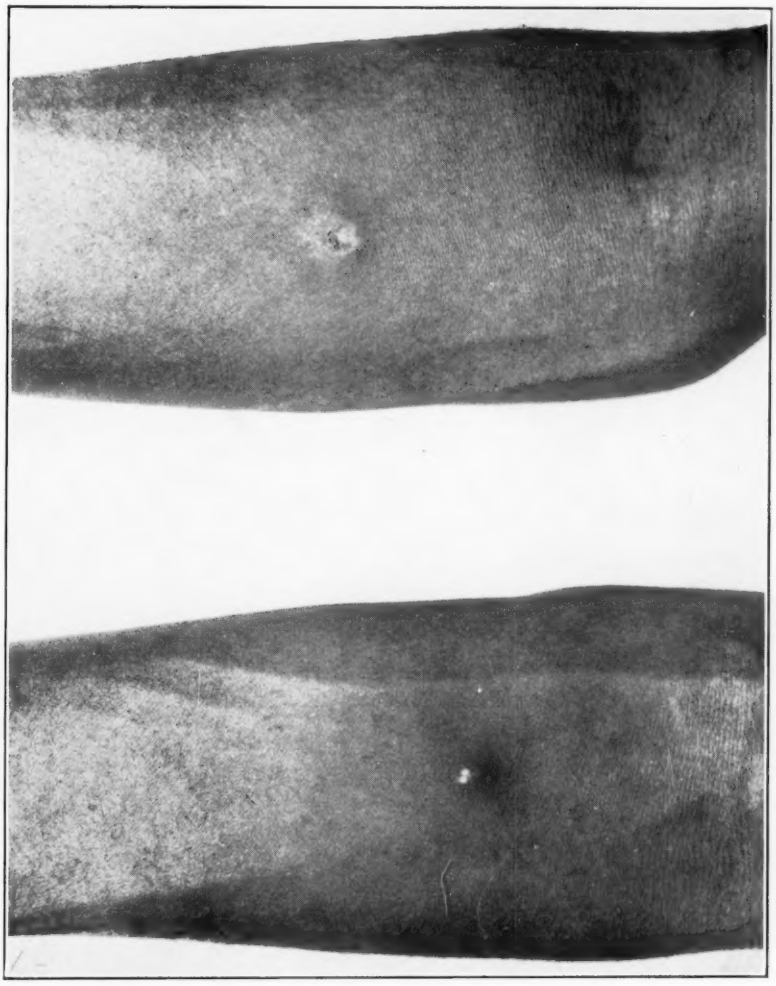

Fig. 9.—A. G., colored female with anal ulcer and fistula and history of purulent discharge from rectum for three years. This shows the pustular reaction and the ulceration as a result of two different Frei antigens given seven days before. A biopsy of the ulcerated lesion is shown in Fig. 13.

If we now consider the two previously mentioned factors, the variation in the patients and the variation of the antigens, and figure only those patients who reacted in a positive manner to 50 per cent or more of the antigens used upon them, and only those antigens which gave

TABLE IV

I. INGUINAL ADENOPATHY GROUP

	A1	A2	A3	A5	A9	A10	A13	A14	A15	A16
1. E. F.	–	–	–x			–			xx	
2. R. C.			x	x				–		–
3. O. O.		xx	xx				–	–	–	–
4. A. B.					x					x
5.			xx							x

TABLE V

II. GENITOANAL SYNDROME GROUP

	A1	A2	A3	A4	A5	A6	A7	A9	A10	A11	A12	A13	A14	A15	A16
1. J. M.	x	xx	– –x	x	x			–				–			x
2. L. M.	– –	– –	–	xx–x						–			–		
3. E. C.		xx	xx	xx	x	x	–						–		
4. E. R.	x	–				–	–								
5. Q. S.		xx	xxx	x	–			–	–				–		–
6. A. G.		x	xx		x	x		–		–	x	–	–		x
7. F. W.	–	xx	–	x		x		–	x–						
8. L. E.			xx		x										
9. D. J.					–										xx
10. M. B.			x												x
11. E. A.			x												
12. L. R.			xxx	x	x					x			x	–	xx
13. G. S.				x	x										xx
14. A. R.		–								x					
15. L. S.			xx	x	–										x
16. P. D.			–												x
17. C. L.	x	– –x	– –	–	– –					xxx			–		–
18. R. B.		x	x												
19. L. B.		–	–	xx	–								–		x
20. J. M.		x	xxx		–			–	–			x	–	–	

TABLE VI

III. RECTAL STRICTURE GROUP

	A1	A2	A3	A4	A5	A6	A8	A9	A10	A11	A12	A13	A14	A15	A16
1. M. W.	xx	x	xx		x				–	x		–		–	x
2. C. S.	–	–x	x				–		–						
3. J. B.	x	x	x	x	x					– –		–	x	–	x
4. B. H.	x	x			x	x				x		x			x
5. H. P.	–	xx	xx	x	x	– –			x				–		
6. B. T.	x	xx	xx												
7. E. L.	x	x	x							–					
8. M. S.		– –	–	x				– –							
9. C. J.	–									–					
10. G. W.			xx			–				x					
11. M. H.		x	xx												
12. A. J.	–	xx	xx												
13. I. Q.										x					
14. J. A.		x						x			–				x
15. R. L.		x	x												
16. N. M.	x	xx	xx	x	x	x		x			–	xxx–			x

TABLE VII

IV. URETHRAL SYNDROME

	A2	A3	A5	A13	A14	A16
1. L. C.	x	xx	–	x	x	x

TABLE VIII

ANTIGENS	AGE OF ANTIGENS	SOURCE	DILUTION OF ANTIGEN	NO. TIMES USED	POSITIVE TESTS	PER CENT POSITIVES
A1	3 yr.	B. pus*	1:10	18	10	55
A2	1 yr.	B. pus	1:10	41	30	73
A3	Fresh	B. pus	1:20	58	48	82
A4	1 yr.	B. pus		19	17	89
A5		B. pus	Poly #6†	20	12	60
A6	Fresh	B. pus	Poly #5	9	5	56
A7	1 yr.	B. pus	Poly #4	2	0	0
A8	6 mo.	B. pus	Poly #3	1	0	0
A9	3 yr.	B. pus	1:10	10	3	30
A10	3 yr.	B. pus	1:10	8	2	20
A11	1 yr.	B. pus	1:10	15	9	60
A12	2 yr.	Bubo		3	1	33
A13	Fresh	Fistula	1:10	12	6	50
A14	Fresh	B. pus	1:5	13	3	23
A15	2 yr.	Perineum		7	2	28
A16	Fresh	B. pus	1:5	24	20	87

*B. pus, refers to inguinal bubo pus.

†Poly No. 6, etc., refers to antigens made from that number of different individuals, and is from bubo pus.

50 per cent or more positive tests of the total number given, we get the following results for the 42 patients studied:

Inguinal adenopathy group	80 per cent positive
Genitoanal group	80 per cent positive
Rectal stricture group	87 per cent positive
Urethral syndrome (1 case)	100 per cent positive
Total for entire group	83 per cent positive

PATHOLOGY

As with so many other phases of lymphopathia venerea, there has been much discussion in the literature as to the microscopic findings in this disease, and with no apparent unanimity of opinion. For the most part, whether the section be from an inguinal gland, a fistulous tract, or a rectal stricture, the microscopic appearance is one of subacute or chronic inflammation. Some have said there is a specific arrangement of epithelioid cells about the periphery of individual abscesses which are usually present. However, if sections are made of tissues from the genitoanal region of a patient with definite lymphopathia venerea and compared with similar sections made from a patient known not to have the disease, the microscopic appearance is very much the same (Figs. 10 and 11). A biopsy of a positive Frei test reveals only a nonspecific inflammatory process (Figs. 12 and 13).

DISCUSSION

If we are to consider the Frei test as a definitely specific means of diagnosing lymphopathia venerea, it then becomes evident that the

disease is much more prevalent than we had previously considered it to be, especially in the colored race. This is particularly true in that group of cases which present nothing more than anal fistulas, anal ulcers, pruritus ani, anal condylomas, etc. However, it is question-

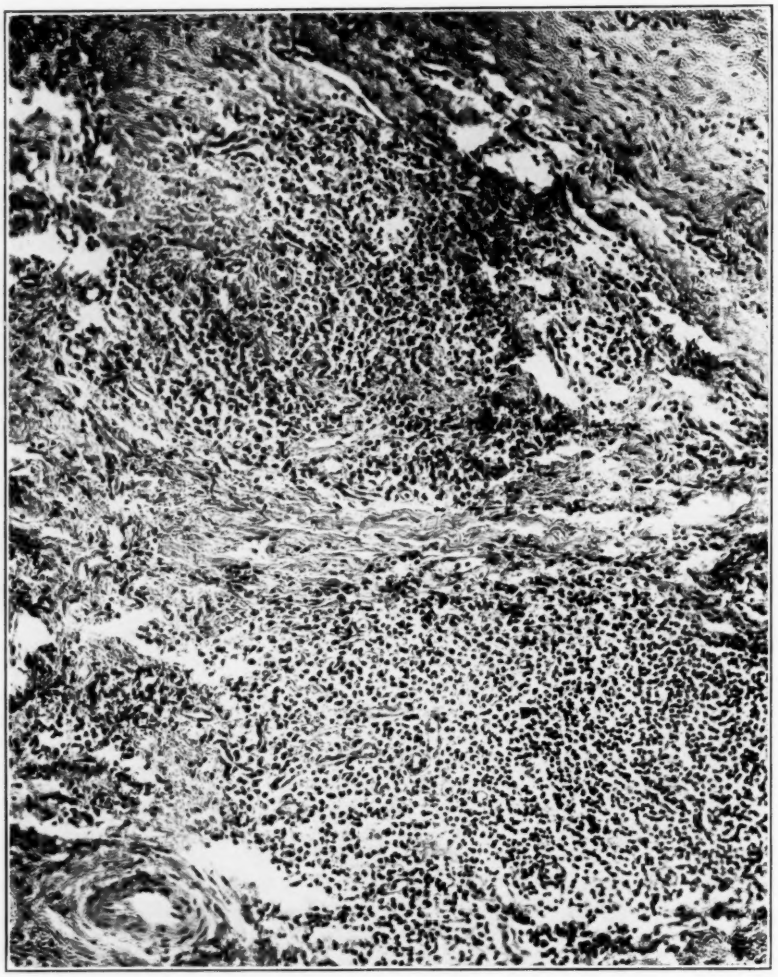

Fig. 10.—Photomicrograph of section from anal fistula in colored female who was considered to have lymphopathia venerea.

able if the Frei test is sufficiently specific to be used as a routine method of diagnosis, unless one remembers and considers the various factors which alter, or may alter, the results obtained. Whether a Frei test will be positive or negative may depend upon any one of the following conditions: the presence of active syphilis; variations in the potency of different antigens; variations in the reaction of patients; presence of other diseases, such as chancroid, active tuberculosis, and high fever;[2] and bacterial contamination of antigens. It

would seem, therefore, unwise to say that any condition suspected of being lymphopathia venerea is such, or is not, simply on the basis of one, or two, or even three Frei tests.

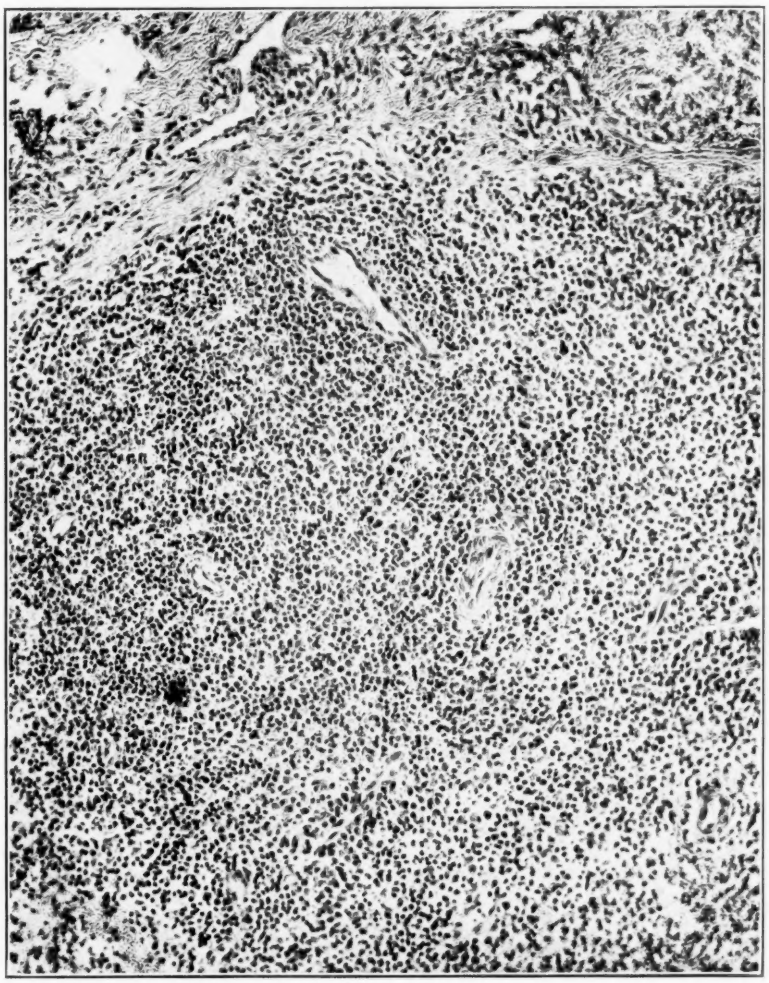

Fig. 11.—Photomicrograph of section from anal fistula in a white female not considered to have lymphopathia venerea. Note the similarity to Fig. 10.

CONCLUSIONS

1. The symptoms and clinical manifestations of lymphopathia venerea may be grouped into four major syndromes: inguinal adenopathy, genitoanal, rectal stricture, and urethral.

2. A single Frei test is not at all specific as a diagnosis of lymphopathia venerea.

3. If a number of different Frei antigens are used upon the same individual, the results may be considered as fairly accurate, and only then should the Frei test be considered as a specific test.

4. Lymphopathia venerea is apparently not a "wastepaper basket" term, for, of the 42 patients with genitorectal conditions studied, approximately 80 per cent were Frei positive.

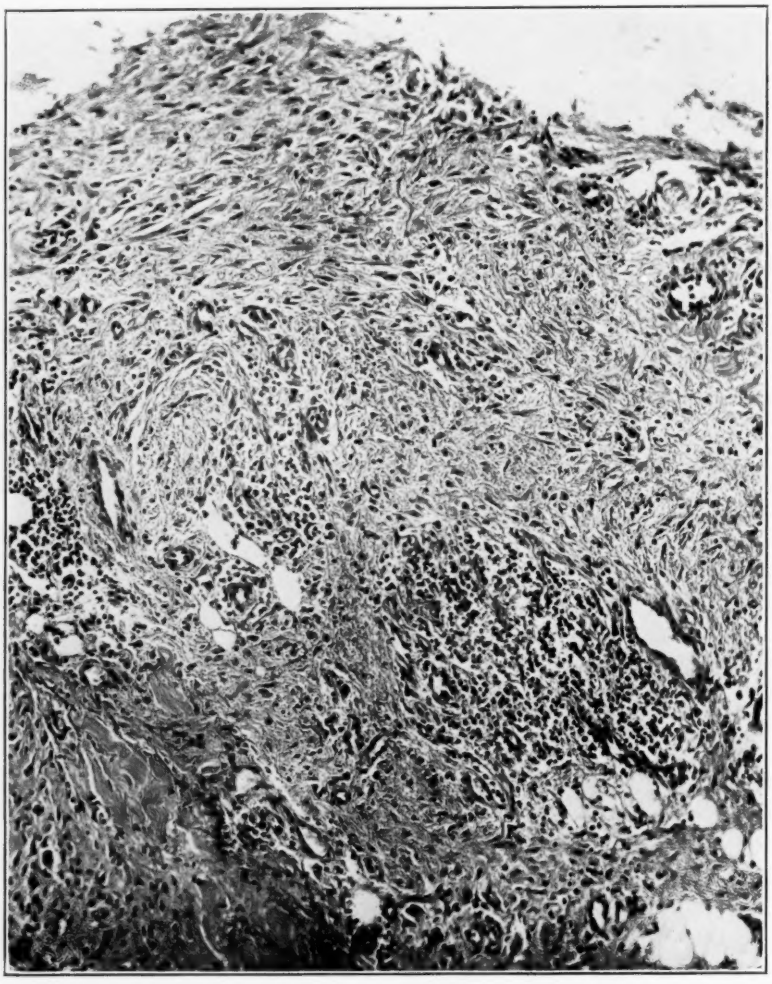

Fig. 12.—Photomicrograph of Frei test. As in Figs. 10 and 11, the main pathology is simply an infiltration of the subcutaneous tissue with numerous plasma cells, neutrophiles, and a few eosinophiles.

5. On the other hand, it is questionable if all rectal strictures will be found the result of lymphopathia venerea if the Frei tests are carefully checked and rechecked. I refer particularly to those who would contend that 95 to 100 per cent of rectal strictures occurring in the colored female are due to this disease.

6. Also, it would appear that many of the cases of ordinary fistulas, ulcers, pruritis, etc., especially as occur in the colored race, are the result of lymphopathia venerea.

7. The microscopic pathology of lymphopathia venerea is that of a nonspecific inflammatory process.

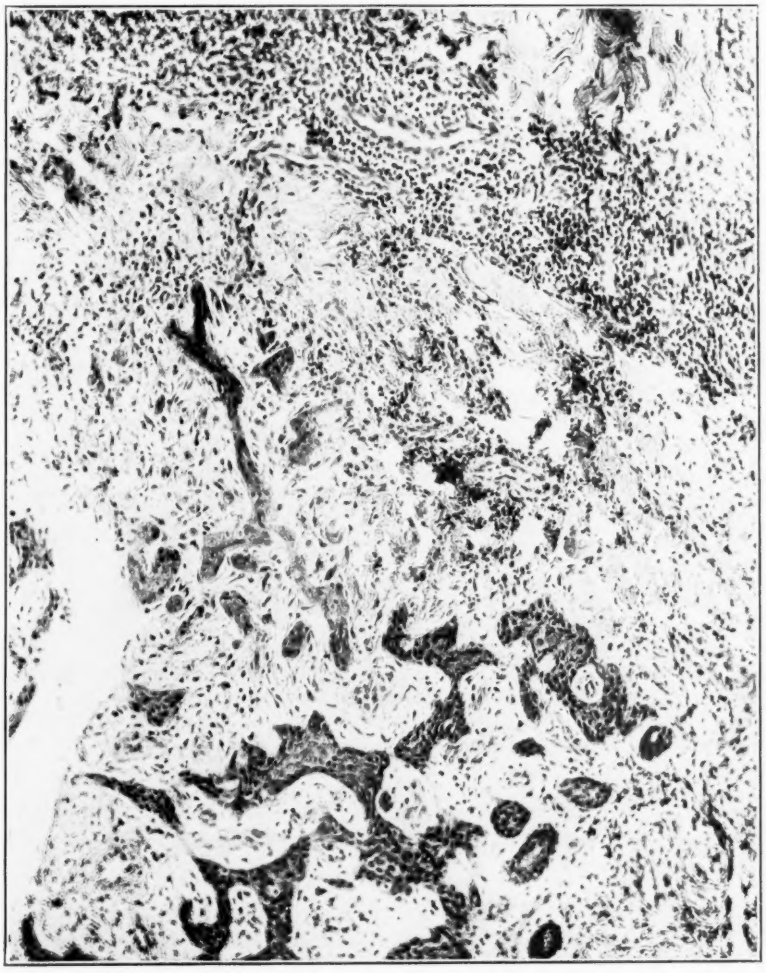

Fig. 13.—Photomicrograph of positive Frei test. Of particular interest in this section, in addition to the cellular infiltration noted in the upper right corner, is the peculiar proliferation of stratified squamous epithelium in the lower portion of the section and which bears a fairly marked superficial resemblance to neoplasm.

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ELIMINATION OF PAIN FOLLOWING HEMORRHOIDECTOMY

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INTRODUCTION

THE general practitioner and surgeon are confronted with few conditions causing more pain, suffering, and postoperative distress than are frequently encountered following hemorrhoidectomy. The laity are often so well "informed" that unnecessary postponement of both rectal examination and operation has naturally followed. To meet the demands of both patient and physician, there has been constant progress made toward rendering the postoperative phase of hemorrhoidectomy less painful and thereby making rectal surgery more acceptable to both patient and physician.

Oil-soluble anesthesia, originally introduced for the treatment of pruritus ani by Yeomans and co-workers[6] gradually has assumed a definite place in the alleviation of pain associated with anorectal surgery. Many oil-soluble anesthetics are now available and a few remarks will be made regarding them.

OIL-SOLUBLE ANESTHESIA

The introduction of benacol by Yeomans[6] was soon followed by others, notably Gabriel's solution, nupercain in oil;[1] anucain introduced by Gorsch;[2, 3] proctocain, by Morgan;[5] and others.[4] Today there are probably a dozen or more oil-soluble anesthetics on the market and it seems desirable to point out that their indiscriminate use and their toxicity due to improperly selected drugs and unbalanced formulas have led to some undesirable results and adverse criticism. Oil-soluble anesthetics dispensed in ampoules and proved of clinical merit by more than one investigator should be selected. The decompensation products of the oils and alcohols, especially those contained in rubber-stoppered or unsealed bottles, will jeopardize the results of the most meticulous technician.

SELECTION OF ANESTHETIC

A preparation should meet the following requirements: (1) It should be nontoxic. (2) It should produce both immediate and prolonged anesthesia. (3) There should be no delay in healing due to its use. (4) The cost of the solution should not prohibit its use in all classes of patients. If the solution itself meets the above requirements, then its more general use will rest upon the proper selection of cases and the proper technique of injection.

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SELECTION OF CASES

In this particular report oil-soluble anesthesia was used in hemorrhoidectomies only. However, this type of anesthesia can be used in fissures, cryptitis and papillitis, pruritus ani, external thrombotic hemorrhoids and a single uncomplicated combined hemorrhoid amenable to ambulatory operative treatment in selected cases, coccygodynia, and sphincter spasm as will be noted in the numerous references.

In this paper, if we consider the indications for injection to be elimination of pain following hemorrhoidectomy, the purpose has been served.

The object of injecting an oil-soluble anesthetic about the anus and rectum is manyfold. The production of prolonged and profound anesthesia about the anorectum is followed by prolonged relaxation of the sphincter muscles. This is accompanied by a remarkable freedom from postoperative pain and discomfort. If this can be accomplished without interfering with the healing of tissue and without the formation of induration, abscess, fistula, or deformity, we have a distinctly useful procedure in the realm of rectal surgery.

CONTRAINDICATIONS

The important contraindications to injection are hemorrhoids accompanied by active suppuration in the form of abscess, sinus, fistula, and perirectal cellulitis, particularly that encountered in lymphopathia venerea (lymphogranuloma inguinale) of the rectum and anus.

Aged individuals whose sphincter mechanism is somewhat lax and atonic usually dislike the prolonged anesthetic effect as they are partially incontinent for the duration of anesthesia. Diabetics and others whose tissues appear markedly devitalized should be injected with caution and it is advisable to use the weaker solutions in smaller amounts in these cases. Particularly has this been found true for the solutions containing phenol or benzyl alcohol, either alone or in combination. Although this is not shown in this particular series of cases, it is mentioned due to my experience with several hundred injections of oil-soluble anesthesia in other anorectal conditions in which a few complications due to strong solutions or unbalanced formulas were encountered.

TECHNIQUE OF INJECTION

The technique of injection has been particularly well described by Morgan[5] and Gorsch,[2, 3] but for the sake of completeness, the method used in this series will be described.

At the time of operation, following the administration of the general, spinal, caudal, or trans-sacral anesthetic and before any operative procedure is started, the oil-soluble anesthetic is injected. Ten

cubic centimeters of solution is the usual amount used. It is felt that a 2½-inch, 22 gauge needle fitted to a 10 c.c. Luer-Lok syringe with ring handles facilitates a smooth even distribution of the solution. The needle is inserted through the skin in the posterior midline approximately 1 inch distal to the anal margin. The injection is to be given, bilaterally, through two sites of os puncture, one each in the posterior and anterior midline (Fig. 1). Two well defined areas of distribution are used, a superficial and a deep (Fig. 2). No oil-soluble anesthetic should be injected intradermally, as slough will follow.

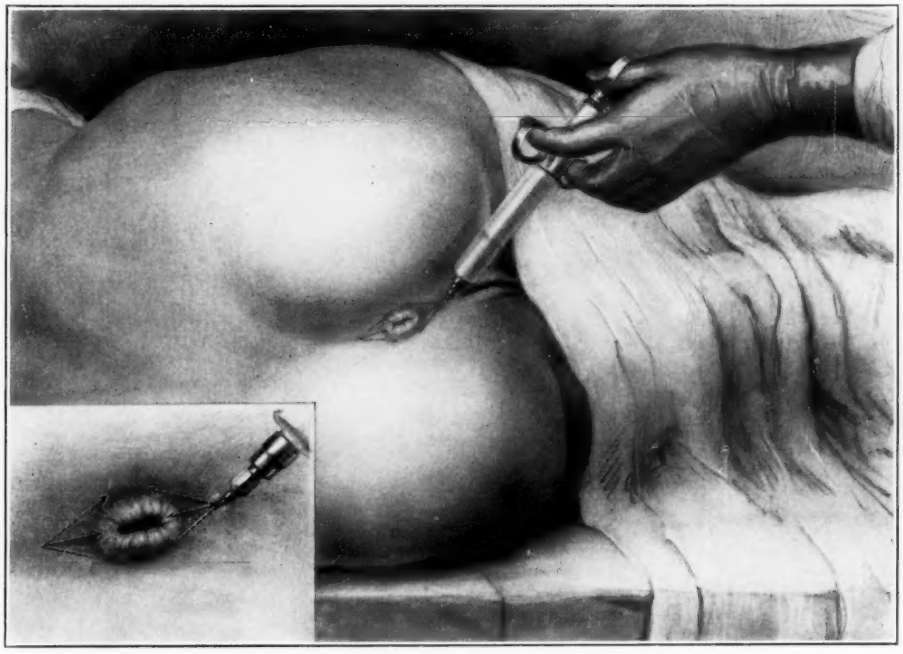

Fig. 1.—Illustrating the site of needle puncture.

The superficial distribution of the oil through the posterior insertion is a perianal infiltration of the subcutaneous tissues around the posterior three-fourths of the anus. About 2 c.c. of solution is thus superficially injected, particular attention being made to place some of it along the lateral margins of the subcutaneous external sphincter muscle. To prevent penetration of the rectal mucosa and to facilitate injection, the index finger is now inserted into the anus and through the same posterior site of injection the needle is guided so as to distribute the solution about the external and lateral margins of the entire sphincter muscles. Insertion of the needle into the tissues for ½ to ¾ inch posteriorly and for ¾ to 1½ inches posterolaterally along the sides of the muscle ordinarily will reach the principal innervation of this area which is from the inferior hemorrhoidal nerves.

Accurate and careful anatomic distribution of the solution is both possible and essential to obtain good results. Approximately 6 c.c. of solution is infiltrated into the deeper tissues in this fashion. The remaining 2 c.c. of solution is infiltrated, both superficially and deep, about the anterior fourth of the anus through a single anterior puncture. The distribution of the solution here blocks off the anal fibers of the perineal nerve which innervates the anterior fourth of the anus.

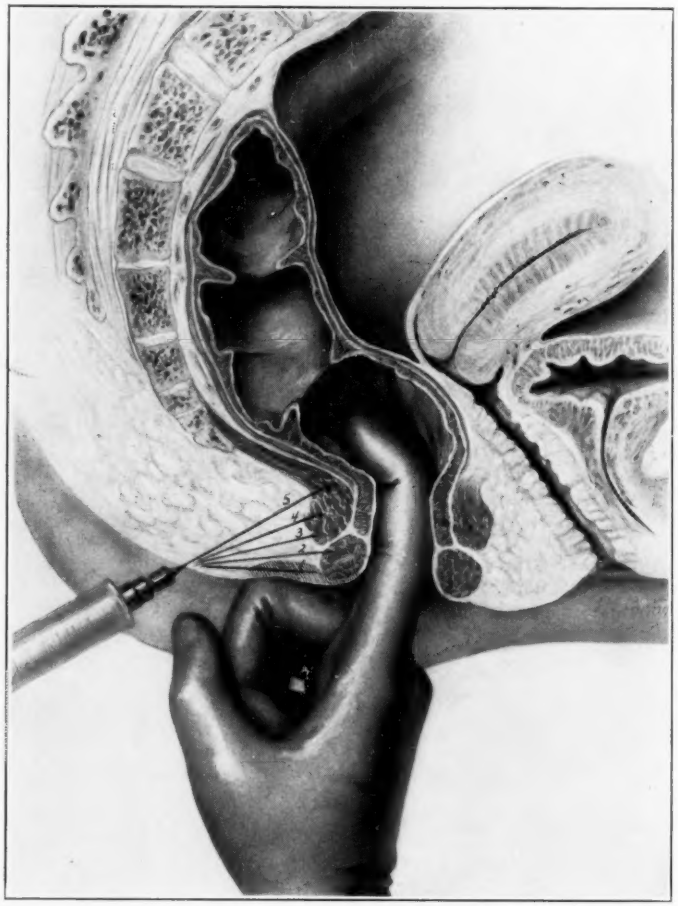

Fig. 2.—Illustrating the superficial and deep planes of injection. The subcutaneous area with the vertical shading shows the plane of injection obtained by inserting the needle along the line marked *1*. The deeper injections are given along the lines marked *2*, *3*, *4*, and *5*.

The simple technique of injection must be strictly adhered to in order to get good results and avoid complications. By using a small gauge needle and keeping it in motion we avoid "pooling" of the solution. Abscess, fistula, and induration are known to follow errors in technique, mainly due to pooling of the solution or perforation of the rectum. Intradermal injection of any of the known oil-soluble anesthetics is invariably followed by slough.

REPORT OF CASES

The same routine preoperative medication with barbiturates and morphine was given in both series of cases. This preliminary preparation in the experience of many has greatly facilitated the administration of a spinal anesthetic.

All patients were given a spinal anesthetic consisting of 90 to 100 mg. of novocain crystals dissolved in spinal fluid.

The Hirschman technique of ligature and excision of the pile mass was used in all patients. A radical hemorrhoidectomy was thus carried out. Clamp and cautery technique was not used in any case. The operative wounds in both series were not closed by suture in any fashion, as the Hirschman technique of operation is an open-wound method that heals by granulation. Suture and closure of the wound is invariably accompanied by more postoperative tissue edema, pressure, stitch infection, and inadequate drainage than the open-wound method. Postoperative spasm of the sphincter muscle which grips the operative wound sufficiently to produce ischemia, delayed healing, and postoperative pain is avoided if one does not stitch any suture material into the muscle where it acts as an irritating foreign body. At the conclusion of the operation, a thin strip of gauze, whose diameter in the anal canal would not exceed that of a lead pencil (often less), was inserted as a dressing in all cases.

The same routine postoperative care using warm compresses, Sitz baths, etc., was carried out in all cases.

The patients were out of bed and up on the second postoperative day, were given full diet from the second day on; had their first bowel movement usually the second day, and were given their first digital examination the third day. Patients on whom this radical type of hemorrhoidectomy was done are requested to stay in the hospital between five to eight days.

Table I shows the amount of narcotics used.

TABLE I

NO. OF DOSES OF NARCOTIC	0	1	2	3	4	5	6	7	TOTAL	AVERAGE
Series I										
Patients not injected	0	0	4	6	14	21	4	1	50 pt.	
Total narcotics	0	0	8	18	56	105	24	7	218 doses	4.03
Series II										
Patients injected	18	16	6	4	3	1	1	1	50 pt.	
Total narcotics	0	16	12	12	12	5	6	7	70 doses	1.4
Series II						50-18 = 32 cases				
Corrected dosage						32 cases : 70 doses				2.18

ANALYSIS OF CASES

The analysis of these two series of cases has considerable comparative value and presents some interesting findings in regard to: (1) the amount of narcotic required to control postoperative pain; (2) the

need for catheterization; (3) the ease of first bowel action; (4) the diminution in pain incident to postoperative digital examination; (5) the extent of surgery done; (6) the complications incident to operation. These will be discussed in order.

1. *The Amount of Narcotic Required to Control Postoperative Pain.*—In Series I, not injected, a total of 218 doses of narcotic were required. The average dose per patient was 4.03. Examination of the chart reveals that the dose range in this group was from 3 to 6. There were no patients in this group who were able to be comfortable without at least one dose of narcotic. The largest number of patients were in the group requiring 4 and 5 doses of narcotic and some of these individuals had nausea and vomiting directly attributable to the morphine.

In Series II, injected, a total of 70 doses of narcotic were required. However, in this series 18 patients (or 30 per cent) did not require any narcotic at any time after operation. This leaves a total of 32 patients (or 64 per cent) of the injected group who required narcotic for the average dose of 2.18. The dose range in this group was from 1 to 4. The largest number of patients were in the groups requiring 1 to 4 doses of narcotic.

2. *The Need of Catheterization.*—In Series I, not injected, 2 patients required catheterization. In Series II, injected, no patient required catheterization.

3. *The Ease of First Bowel Action.*—The usual regime in both series was a rectal instillation of warm oil on the morning of the second postoperative day. While it is impossible to chart the relief of such an intangible subject as painful bowel movement, a vast difference was noted between the two series.

Series I, not injected, had a greater tendency to delay the time of bowel movement. There was rarely a spontaneous action in this group. All had pain at the time of bowel movement and in a large number of patients the pain was more severe and was slower in subsiding.

Series II, injected, had less tendency to delay evacuation. Many had a partial involuntary passage during the first 3 to 5 days, and there were a few whose sphincter paralysis persisted for 12 to 14 days. About 50 per cent of the patients had pain at the time of bowel movement, but the severity of the pain was less and the subsidence of the pain was more rapid than in the other series.

In about 25 per cent of the cases, I would estimate that the pain of first bowel movement would be as severe in this series as it was in the group who were not injected. However, the subsequent passages usually would be much easier. In the entire group, with few exceptions, these patients were more comfortable during the intervals between bowel actions.

4. *The Diminution in Pain Incident to Postoperative Examination.*—This was painful to all patients in both series. It should be understood

that none of these patients had an absolutely painless postoperative course. The absurdity of some writers who publish and tabulate records indicating "no pain after operation" is a rather poor tribute to the average physician's mentality or to the patient's fortitude. I personally made the examinations in this series and know all of these patients had pain during their first digital examination. One thing was definitely noted; that, in general, the severity of the pain was less and the subsidence of the pain was more rapid in the injected group, Series II. In Series I, not injected, the pain was severe, the sphincter spastic, and the aftermath prolonged.

In Series II, injected, the pain was less severe and in many exceptionally mild by comparison. The sphincter was relaxed in all and in about 30 per cent of the cases it was actually gaping and patulous for many seconds after digital examination.

5. *The Extent of Surgery Done.*—In Series I, not injected, the usual technique of operation was used. The pedicle was ligated and the hemorrhoid excised so as to include a generous portion of skin. Hemorrhoidectomy was done in three quadrants in most of the cases and in a very small number excision was carried out in four quadrants.

In Series II, injected, the usual technique of operation was used in the first few cases. As it became more evident that the prolonged muscular relaxation and anesthesia would permit of more thorough postoperative digital examinations, the amount of tissue removed became greater. I would estimate that 70 per cent of cases in Series II had more hemorrhoidal tissue removed than those in Series I. The operation became more radical and it is safe to say the results more satisfactory. The incidence of postoperative skin tags became almost nil, and a smooth anus "without a vein in sight" became the rule. Series II, injected, definitely had a more radical operation.

6. *The Complications Incident to Operation.*—In Series I, not injected, there were 2 postoperative complications. In 1, a small thrombus developed in an island of skin left between the areas of excision. Linear incision of the overlying skin and evacuation of the clot relieved this immediately. One patient developed a sensitive scar which required the injection of a local anesthetic and freeing of the scar about two months after operation. None had developed stricture or abscess and there were no postoperative hemorrhages.

In Series II, injected, there was 1 case of delayed healing accompanied by a marked perianal erythema and pruritic dermatitis medicamentosa due to an idiosyncrasy to the solution. This was confirmed by the patch test. Prolonged sensory anesthesia or muscular weakness should not be considered a complication of these injected cases. This is desirable and constitutes part of the valid reasons for using the solution. However, it should be mentioned that all of these patients were cautioned that when any urge or desire to stool appeared

they should hurry to the bathroom immediately. Particularly was this true during the first week and in a few cases as long as fourteen to eighteen days. All developed normal sensation and muscular function following absorption of the anesthesia.

Although I had a few cases of induration and abscess in other cases, such as fissure and single thrombotic hemorrhoid treated in office practice, there were no such cases in this series. Improper solutions and errors in technique accounted for the above mentioned cases. Except as mentioned, delayed healing did not occur.

SUMMARY

In reviewing the notes on the charts and my own observations on these two series of patients, it was perfectly evident that in Series II, injected, we had a group of patients enjoying postoperative comfort to a degree not approached heretofore. There were many ways in which the daily observation of these injected cases differed from the other series. Patients who are comfortable to the extent of sitting up in bed, reading the paper, and partaking of a full diet on the first or second postoperative day were encountered rather frequently. Nausea, vomiting, and other signs of morphinism were largely eliminated. There were a few whose threshold of pain was not influenced completely by the injection, as indicated by the 32 cases. There were some in this Series II, injected, upon whom the injection of the oil soluble anesthetic seemed to have little effect. This is to be expected in the future. Although this is a small series of cases to report, the author feels that a review of a larger series would yield essentially the same information. The records and observations on these cases have been made personally and have been carefully kept and analyzed.

CONCLUSIONS

The following conclusions seem evident:

1. Oil soluble anesthesia is a valuable and efficient supplementary form of anesthesia available for hemorrhoidectomy.

2. Patients given an injection of oil soluble anesthesia have a more comfortable postoperative period as measured by (1) the amount of narcotic used, (2) the need for catheterization, (3) the ease of first bowel action, (4) the diminution in pain incident to digital examination.

3. Oil soluble anesthesia, properly used, permits of a more radical removal of hemorrhoid tissue, is not attended by delayed healing, and is rarely accompanied by any untoward sequelae.

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MAJOR OPERATIONS IN ELDERLY PATIENTS

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THE surgical care of those in the autumn of life has become a problem of enlarging interest and importance during the last half century because of the ever increasing number of patients over 70 years of age who present themselves for diagnosis and treatment. It is surprising to think that eighty years ago only one-half of our population reached the age of 40 years, while in 1931, as Brooks points out, the average age of of the white male was 59 years and the white female 62 years. In other words, life expectancy has been increased by 20 years during the past eight decades.

Of a population of 122,000,000 in 1931, 6.6 per cent were over 65 years of age, or twice the number living in 1850. With this rate of increase projected over a similar period of years, there will be seven times as many people over 65 years, or about 28,000,000. From another point of view, a brief survey of the vital statistics of the Metropolitan Life Insurance Company is of interest. This shows that out of a group of 1,000 children of 10 years of age, over one-half will reach the 60's, while more than one-third will survive 70. There will be 145 octogenarians, and 8 of these will live for 90 years or more.

Responsible in part for this striking shift of our population is, of course, the medical profession. It has, through a wider distribution of intelligent medical care, created a responsibility which, although it may be a privilege to enjoy, is notwithstanding an enormous obligation.

First among the American writers to express an interest in the health of the aged were Chaveat and Loomis, who, in 1881, published a book on *Diseases of Old Age*. Nasher followed their example in 1912, while Thewlis made his valuable contribution to the subject in 1919. During the past twenty years many interesting and instructive articles have appeared which show an increasing interest in this growing problem of the surgical care of the aged. As Morten points out, the urologists were, by dint of sheer necessity, the first to realize the ability of the aged to withstand surgery with a surprising degree of resistance and in the face of the gravest physiologic adversities. Gradually, experience has shown that old age is no longer the contraindication to surgery that it was at the beginning of the century, and more and more data are being accumulated to substantiate this fact. Lazarus reported a case of a woman 85 years of age upon whom he had operated successfully for a ruptured, gangrenous appendix; Horsley

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has successfully resected the stomach for cancer in five patients over 70 years of age; Mayo and Nettrour have reported an interesting series of major surgical procedures in patients over 70; Yeomans and Newton, of Australia, each have reviewed a series of 100 such cases; Brooks, of Nashville, Tenn., discussed a group of 287 surgical cases over 70 years of age treated at the University Hospital during the ten-year period following 1925; and Gordon-Taylor states that to his knowledge the oldest person to be successfully operated upon was a 106-year-old woman who had a strangulated femoral hernia.

It was Osler's opinion that a deficient circulatory system is the true measure of old age, and, as is so often observed, some persons 50 years of age seem older than others of 70. However, tradition has it that the allotted span of life is three score years and ten, therefore those beyond this arbitrary point shall be considered in the old age group. Many who attain this age are alert, intellectually active, and anxious to live. They seek the surgeon in the hope that something may be done for them and are in a more receptive frame of mind when surgery is indicated. There is less interference from superstition, prejudice, and fear. From the surgeon's standpoint, pre- and postoperative care, technique, and anesthesia combine to afford the patient a far better prognosis than in the days of the frock coat and carbolic acid spray. However, due credit must be given these people, for without a sturdiness of fiber they would never have reached the age of 70 years. The end result is a steady increase in the operability of patients in this group with a concomitant fall in surgical mortality.

To assume this responsibility with credit to the profession, a carefully coordinated series of meticulously arranged details must be carried out with a precision and deftness that can be acquired only through a well-rounded surgical training and seasoned experience. The nicety of surgical judgment as to when, what, and how much to do is the keynote to success in these patients. It is, however, a futile attack unless adequately flanked and supported by thoroughly capable pre- and postoperative care.

A prompt and accurate diagnosis, of course, is essential, but here the examination has just begun. A searching study of the most intimate details of the patient's physiologic state must be made for these patients suffer from the burden of time and scars of previous disease in addition to the illness for which they present themselves. It is therefore important to evaluate as carefully as possible their reserve not only in order to determine their surgical limitations, but also to anticipate and thereby forestall any complications which may develop during the postoperative course, for, as Crile has observed, these complications are best treated before they arise.

PREOPERATIVE PREPARATION

The period of preoperative preparation is, of course, variable, depending upon whether elective or emergency surgery is to be done. However, every effort must be made to capitalize on what few natural resources the patients have managed to retain. No trouble must be spared in attempting to rehabilitate these elderly people as thoroughly as possible, for attention to such details may mean the difference between success and failure. There is no single group of patients in which, as Guthrie suggests, optimism, cheerful encouragement, and subtle management are so absolutely essential. Regimentation and the domination of a relentless and impersonal routine, or the sudden changes to which old people cannot adjust themselves readily, may be the sole cause of miserable failure. The aged frequently have accustomed themselves to reign supreme, and to thwart their harmless whims creates unnecessary conflict. On the other hand, and even more difficult to contend with, are a certain few who seem overpowered with a sense of hopeless futility. A prelude of soft restraint and gradual readjustment to surroundings and routine is, in elective surgery, as important as a cheerful attending staff of doctors, nurses, and visitors; while comfort, and pleasant food and quarters add materially to the *joi de vie* which must be infused into the patients.

Careful oral hygiene not only will increase dietary efficiency, but may prevent a not infrequently fatal postoperative parotitis. A well-rounded, high caloric diet, adequately supplied with vitamins and easily assimilated carbohydrates, will replenish any possible deficiency and re-establish a depleted glycogen reserve. Hydration with from 3,000 to 4,000 c.c. of fluid with an accurate record of the output will determine the water balance. Ten per cent glucose intravenously is the most efficient mild diuretic which may be used to combat an inadequate urinary output with a rising blood urea. It is also a valuable cardiac nutrient as well as a liver protective, although, of course, intravenous therapy must be governed by cardiac efficiency and limited at the first suggestion of decompensation. The correction of anemia not only will relieve the heart of a notable burden produced by inadequate oxygenation, but will restore it to more nearly normal the physiologic processes of these old people which, at best, function only at minimum efficiency.

If there is a previous history of cardiac decompensation or if electrocardiography reveals evidence suggestive of myocardial damage which under the additional strain of surgery may lead to heart failure, the question of preoperative digitalization presents itself. Inadequate digitalization is of no therapeutic value, and complete digitalization should be instituted only in the face of impending failure or actual decompensation. In the presence of such a complication, surgery is to be deferred when possible; otherwise prompt digitalization is the

procedure of choice. Obviously, the earliest postoperative evidence of decompensation is an indication for digitalization. The usual preoperative measures, such as cleansing of the colon, or gastric lavage, in surgery of the large bowel, or stomach, are such routine measures that they hardly need be mentioned here.

Laplace and Nicolson have studied the effect of prolonged recumbency in 34 patients confined to bed for orthopedic treatment who were otherwise in good health. One-half of these patients died, but of these 17 in only 10 was death directly attributable to prolonged confinement. These authors show that the continued inactivity of old patients confined to bed leads to a circulatory retardation with peripheral stagnation which is closely analogous to shock and that "local anoxemia and consequent degeneration of tissues leads to toxemia and to permanent capillary damage which perpetuates the circulatory fault and ultimately results in death." These conclusions obviously favor as short a period of recumbency as possible, with active or passive muscular exercise. Whenever practical, preoperative patients should be encouraged to be up and around during their preparation for surgery, and postoperative patients are to be mobilized as soon as possible.

ANESTHESIA

The question of anesthesia in the aged is still a problem open to discussion, but upon one point there is unanimous agreement; the anesthetist must be a good one. With this as a major premise, we find cause for a great diversity of preference among different surgeons. Thompson and Habein, in their series of 1,200 urological patients over 70 years of age, used spinal anesthesia almost exclusively. Keynes is partial to nitrous oxide and oxygen alone or in combination with avertin in elderly people, but he emphasizes the value of infiltration anesthesia. Crile disapproves of avertin or ether, but favors local anesthesia and uses spinal anesthesia regardless of the patient's age whenever sufficient blood can be given preoperatively. In Newton's series of 100 cases of major surgery in patients over 70 years of age, general anesthesia was used except in an occasional case in which there were obvious indications for local anesthesia. Nitrous oxide or ethylene was his choice whenever possible.

TABLE I

ANESTHETIC

TYPE	NO. OPERATIONS	PULMONARY COMPLICATIONS	PERCENTAGE
Gas-ether	26	2	7.6
Gas-local	4	1	25.0
Local	21	4	17.2
Sacral	4	0	0
Total	55	7	12.7

In our series of 44 cases subjected to 55 operations, gas-oxygen-ether was used in 26 cases; local anesthesia was chosen in 21, sacral anesthesia proved satisfactory in 3 posterior resections of the rectum and in 1 vaginal hysterectomy; while local anesthesia supplemented with gas was used 4 times. Postoperative pulmonary complications occurred in 7 cases. One patient, with an ileocolostomy, died seventeen days postoperatively with bronchopneumonia; the anesthetic had been gas-ether. A second death from bronchopneumonia occurred four days after a secondary closure for wound disruption, done under local anesthesia. A third patient, an appendectomy done under gas-ether, developed a small area of bronchopneumonia six days postoperatively, but recovered. A fourth patient had a closure of a colostomy and amputation of the penis for cancer, done under local anesthesia at one time, and developed a mild bronchopneumonia; while in a fifth patient a small area of bronchopneumonia appeared on the fourth postoperative day following removal of a ruptured appendix under local anesthesia supplemented with gas. The only case of atelectasis followed a hernioplasty, done under local anesthesia. A sixth case died of bronchopneumonia on the sixteenth postoperative day following exteriorization of an esophageal diverticulum, under local anesthesia. The one death from pulmonary embolism had no relation to anesthesia and therefore will not be discussed with this group. In other words, the instance of postanesthetic pulmonary complications following 55 operations was 12.7 per cent. Of these, 2 occurred in the series of 26 which were given gas-ether, an instance of 7.6 per cent; while 4 followed the use of infiltration anesthesia in a series of 25 cases, a percentage of 16.8. Four of the infiltration anesthetics were supplemented with gas, with but 1 postoperative complication, an incidence of 25 per cent. Although this is not a large series, it shows conclusively that a good anesthetist, a short operative time, and careful postoperative care will render the use of general anesthesia in old people as safe as any other anesthetic available.

SURGICAL OBSERVATIONS

From the standpoint of technical accomplishment, it is perhaps superfluous to repeat that judgment, speed, and gentleness compose the essential triumvirate for surgical success in these old persons. Little need be said about gentleness and speed except to emphasize that both tend to avoid shock as well as minimize the depth and duration of anesthesia, all of which have an extremely important bearing on the postoperative course. With regard to judgment, so many factors are involved that it cannot well be discussed in detail. Briefly, however, it is a question of how much surgery these patients can stand. Frequently this brings up the point of whether it is wiser to perform a single- or multiple-stage operation. Cohen has noted that secondary operations in these

patients most often prove fatal and therefore he condemns the multiple-stage procedure. C. W. Mayo reported 4 cases of patients over 70 years of age who underwent multiple-stage operations with success. In this series, 7 patients were operated upon two or more times, without mortality. Naturally it is unwise and unjust to prolong the period of invalidism unnecessarily by subjecting a patient to a series of surgical procedures when the same end can be accomplished without undue danger at one operation. However, these findings would suggest that multiple-stage operations may well be carried out upon elderly patients and that in those of questionable surgical tolerance it is perhaps best to err on the side of conservatism. A period of from two to three weeks or longer may be necessary between stages. Every effort must be made at rehabilitation before subjecting the patients to further surgery, so not infrequently the interval is prolonged. It is seldom that one or two additional weeks, during which time the patient may be up and around or even leave the hospital, will not be of material benefit.

POSTOPERATIVE CARE

Bodily warmth must be maintained during the transfer from the operating room to the bed on the ward. Patients should be turned frequently and inhalations of carbon dioxide, after the method of Graham, should be routine procedure. Deep respiratory excursions tend to aerate the bases of the lungs, which in old people are frequently congested or partially atelectatic, and in this way help to prevent pulmonary complications, which, as Harvey has said, occur six times more frequently in patients over 65 years of age than in those in the prime of life. Morphine is best used sparingly due to its depressing effect on the respiratory center and the cough reflex. Atropine in conjunction with it tends to decrease bronchial secretions and thereby facilitates a more complete aeration of all parts of the lungs. Pain, restlessness, and apprehension must be controlled, but with minimum sedation. The barbiturates are often poorly tolerated by old people and their effect is at times accumulative. This may serve to mask the early signs of renal insufficiency. The matter of hydration has been sufficiently discussed.

Postoperative transfusions are of importance in replacing blood loss, but a most striking effect may be seen in those patients who have lost momentum and for no specific reason are slowly but steadily failing. Massage of the extremities as well as active and passive exercise help to stimulate peripheral circulation and should be started as soon as practicable, to be repeated at regular intervals. Whittaker reported the case of an octogenarian who, following a gastroenterostomy, was gotten out of bed and allowed food on the third postoperative day.

CLINICAL SURVEY

In this series of 44 patients over 70 years of age who have undergone major surgical procedures, it was found that 29 patients were between 70 and 75 years of age, while 15 were from 75 to 82: Average age, 73.5 years; oldest patient, 82 years; patients 70 to 74 years old, 29; patients 75 to 80 years old, 12; patients above 80 years, 3. Only 3 patients had passed the age of 80 years, and of these the oldest was 82. The average age of the group was 73.5 years.

TABLE II

TYPES OF SURGERY

Elective operations	48	Malignant disease	24
Emergency operations	7	Benign disease	20
Colon and rectum	16	Pelvic	2
Biliary tract	7	Breast	4
Hernia repair	5	Exploration	1
Upper gastrointestinal	4	Appendix	3
		Miscellaneous	2

There were only 7 emergency operations performed in this series, while 54.5 per cent of the cases suffered from malignant disease. There were 16 colon and rectal cases, of which 14 were referred for carcinoma. One patient was found to have a carcinoma of the right colon. There were 8 cases of carcinoma of the sigmoid, while 5 patients suffered from cancer of the rectum. One patient had a diverticulitis of the sigmoid and another a lipoma of the mesentery of the sigmoid.

In 5 cases of malignant disease of the large bowel nothing more than colostomy could be done. Colostomy with subsequent posterior resection was performed in 3 cases, while an obstructive resection with complementary cecostomy was done 3 times. Ileocolostomy and right colectomy were performed in 1 case, and exteriorization for cancer of the sigmoid was accomplished in 2 cases. This latter procedure was likewise used in 1 patient with a lipoma of the mesentery and another suffering from diverticulitis.

Of the 7 cases operated upon for disease of the biliary system, 2 patients explored were found to have inoperable carcinomas, 1 of them having a cancer of the gall bladder, while the other was found to have a carcinoma of the liver, thought to be primary. Four patients were operated upon for inflammatory disease of the gall bladder with stones, and another, suffering from a painless, progressive jaundice, recovered following a cholecystgastrostomy.

Of the 5 hernias, 1 of the 4 inguinal hernias was strangulated, while the fifth was a large incarcerated multilocular postoperative ventral hernia. Of the 2 pelvic cases, 1 patient had a large ovarian cyst,

which was removed without difficulty, while the other, having a complete prolapse of the uterus, underwent a vaginal hysterectomy, followed by an uneventful recovery.

Three radical amputations of the breast were performed for carcinoma and 1 simple mastectomy was done for a papillary cystadenoma. One patient subjected to laparotomy was found to have an abdominal carcinomatosis, the origin of which could not be determined. Of the 7 cases of appendicitis and upper gastrointestinal tract surgery, 3 suffered from acute appendicitis, 2 being extremely acute, while the third was ruptured with an early peritonitis. One patient had an uneventful recovery following a radical resection of the stomach for a pyloric carcinoma, while a second patient with a cancer of the stomach died of a cerebral accident on the eleventh day following a radical resection. Another suffered from a perforated gastric ulcer for which closure and a posterior gastroenterostomy were performed. Recovery in this case was marred only by a transitory urinary obstruction from a benign prostatic hypertrophy. The last of this group was a patient with an esophageal diverticulum who died on the thirteenth postoperative day of bronchopneumonia following exteriorization of the diverticulum. One patient suffering from a mixed tumor of the parotid gland was operated upon successfully, while a second patient (82) with a cancer situated just anterior to the right tonsillar fossa underwent ligation of the right external carotid artery without mishap.

COMPLICATIONS

Of the 44 patients operated upon, 17 developed one or more postoperative complications, an incidence of 38.6 per cent.

TABLE III

POSTOPERATIVE COMPLICATIONS

Incidence 38.6%			
Total cases	17	Total complications	23
Bronchopneumonia	6	Cystitis	2
Acute retention urine	3	Atelectasis	1
Wound infection	3	Parotitis	1
Wound bleeding	2	Fecal fistula	1
Intestinal obstruction	2	Apoplexy	1
Pulmonary embolism 1			

The commonest of these complications was, of course, bronchopneumonia, which occurred in 6 patients and was responsible for 3 deaths. Acute urinary retention from benign prostatic hypertrophy occurred in 3 cases. Wound infection followed 3 operations, while wound bleeding of moderate severity occurred in 2 of the infected cases, due to erosion of a small vessel. Postoperative intestinal obstruction occurred in 2 cases and was responsible for 1 death. Cystitis, a not infrequent complication following colon surgery, was present in only

2 instances. Pulmonary embolism, cerebral apoplexy, atelectasis, parotitis, and fecal fistula were responsible in 1 instance each. Recovery was complete in all but 6 of these patients.

TABLE IV

MORTALITY

Patients	44	Operations	55
Males	27	Females	17
	Deaths	6	
	Mortality by patient	13.6%	
	Mortality by operation	10.9%	

In this series 6 patients died, an actual mortality of 13.6 per cent; or mortality by operation of 10.9 per cent. This compares favorably with statistics on this age group reported by other observers.

TABLE V

AGE	SEX	DIAGNOSIS	OPERATION	CAUSE OF DEATH	POST-OPERATIVE DAY
72	M	Cancer of the rectum	Colostomy	Intestinal obstruction	12
78	F	Cancer right colon	Ileocolostomy and resection right colon	Bronchopneumonia	17
71	M	Cancer rectosigmoid	(1) Obstructive resection	Bronchopneumonia	12
			(2) Secondary closure for wound disruption		21
73	M	Cancer of the sigmoid	Colostomy	Pulmonary embolism	
71	M	Diverticulum of esophagus	Exteriorization	Bronchopneumonia	13
72	M	Cancer of the stomach	Gastric resection	Apoplexy	12

Our first death occurred on the twelfth postoperative day from an intestinal obstruction following a colostomy in a 72-year-old male operated upon for cancer of the rectum. The second occurred on the seventeenth postoperative day following an ileocolostomy and resection of the right colon for cancer in a 78-year-old white woman who developed a bronchopneumonia. The third death was also from a bronchopneumonia developing twelve days after a secondary closure of a wound disruption which followed an obstructive resection and cecostomy for cancer of the sigmoid. The fourth occurred on the twenty-first day following a colostomy for cancer of the rectum. This patient died from a pulmonary embolus. The fifth patient, operated upon for an esophageal diverticulum, died on the thirteenth postoperative day from bronchopneumonia. The last death occurred on the twelfth day of an unusually smooth convalescence following a resection of two-thirds of the stomach for carcinoma. This patient suffered a cerebral accident and died immediately.

FOLLOW-UP

In the group of 16 colon cases, 4 died in the hospital and, of the remaining 12, 3 were found on exploration to be inoperable; therefore, only a colostomy could be done as a palliative measure. One of these patients is living six months after operation, while the other 2 died at four and nine months respectively. Of the 3 cases in which colostomy and posterior resection were performed, 1 is living and well after one year, another dead of apoplexy twenty-one months postoperatively, while the third lived for two years, to die of a recurrence of the malignancy. Of the 3 patients who survived cecostomy and obstructive resection, all are living and well, 2 at four and twenty-three months respectively; while the third has passed the five-year postoperative mark. Of the 3 patients upon whom exteriorization was performed, 2 are living and well at nine and fourteen months, while 1 died of unknown cause three months postoperatively.

Of the 7 cases of biliary disease, 2 were found to have inoperable malignancies and both died within two months of operation. The remaining 5 were living and well at intervals ranging from nine months to five and one-half years. Of the 5 hernia cases, 4 patients are living and well from five months to four years postoperatively, while 1 patient died four years after operation of an unknown cause. In the group of 4 upper gastrointestinal cases, 2 patients were included in the hospital deaths; 1 patient operated upon for cancer of the pylorus died of a recurrence twenty-five months postoperatively; the patient operated upon for perforated gastric ulcer is living and well four months after operation.

The patient upon whom a vaginal hysterectomy was performed for a prolapsed uterus is living and well at three and one-half years, while the second patient operated upon for a large ovarian cyst is living and well at nine months. Two patients who underwent radical mastectomy for cancer of the breast have died, 1 five months postoperatively with a recurrence, while the second died of dysentery after twenty-six months; a third is living without recurrence at seventeen months, while the patient upon whom simple mastectomy was done for chronic cystic mastitis is well after sixteen months.

Two patients operated upon for acute appendicitis are living and well after six months to three years postoperatively, while the third died of heart disease three years after operation. One patient, who was found at exploration to have a widespread abdominal carcinomatosis, died within a month of operation.

Of the last 2 cases, 1 was operated upon for a mixed cell tumor of the parotid and is living with a recurrence after four years; while the patient in whom ligation of the external carotid artery was performed for cancer of the tonsillar fossa is living two months after operation.

Of the 24 cases of malignancy, 8, or one-third, were found to be inoperable. Palliative procedures only could be used to aid these people. Two remain alive, the other 6 having died, the average length of life after operation being 3.1 months. Five cases of malignancy died in the hospital. Of the remaining 11, 3 who underwent radical surgery have died of a recurrence five, twenty-one, and twenty-five months after operation. Two patients who were subjected to surgical extirpation died twenty-one and twenty-six months afterward of causes unrelated to their previous illnesses.

Six patients, or one-fourth of the original group suffering from malignant disease, have survived radical operations for an average of 25.8 months without evidence of recurrence, which is in contrast to an average postoperative period of 3.3 months in patients upon whom palliative surgery alone could be performed.

Of the 20 cases suffering from nonmalignant disease, 18 are now living and well; therefore, of the entire group operated upon during the past five years, the average length of life has been 21.1 months, ranging from 6 weeks to 5 years. Of the 24 patients now living and well, the average length of postoperative life has been 16.9 months.

SUMMARY

1. The life expectancy of our population has been increased greatly during the past eight decades. There were 8,052,000 people over 70 years of age in our country in 1931 and this number is steadily increasing.

2. Much evidence has accumulated to show that elderly people tolerate surgery surprisingly well. There is a progressive increase in operability with a concomitant decrease in mortality in this age group.

3. Careful preoperative regulation and preparation are of vital importance in the success of surgery in these people. A thorough preoperative study aids materially in the management of postoperative care.

4. Of 55 anesthetics, 28 were gas induction ether; the rest were infiltration anesthetics, supplemented in 3 instances with gas. The postoperative pulmonary complications after ether were 2 as opposed to 5 following infiltration. The secret of this success is due to an extremely good anesthetist.

5. Upon surgical judgment depends the matter of when, what, and how much to do. The question of single- or multiple-stage procedures presents itself and the time interval between stages is discussed.

6. Postoperative care must be as meticulous as the preoperative preparation in order to forestall complications whenever possible, but they must be treated promptly and vigorously when they do occur.

7. A clinical survey of 44 patients over 70 years of age who underwent 55 major surgical procedures is discussed, with reference to types of surgery, postoperative complications, mortality, and end results.

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A REVIEW OF WOUND HEALING AND THE MECHANICS OF DEHISCENCE

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FOR the past several decades the subject of wound dehiscence has found its way into the surgical literature with increasing frequency. It is only too apparent, after reviewing the reports, that this influx is due not to an increase in the incidence, but rather to an alertness by surgeons to an existing hazard. The sad commentary on its present status is the fact that the literature continues to report its incidence relatively unchanged.

In the present article I make no claims for original research. The only justification for it is to review some of the previous literature on the subject, to publish a series of cases illustrating its occurrence, and to analyze both the literature and these case reports of wound dehiscence in an effort to arrive at a more tangible means of eliminating this postoperative complication.

Incidence.—One advantage of this report over several of its predecessors is its accuracy so far as the incidence of eventration is concerned. The time element in this series of cases is sufficiently short to permit a vivid recollection of the details, thereby repudiating the criticism given to several other authors that their records were only as infallible as the record room from which they were obtained.

During the one-and-one-half-year period beginning Jan. 1, 1937, and terminating July 1, 1938, there were 2,526 intraperitoneal operations performed at the Flower and Fifth Avenue Hospitals. During the same period, there were 13 cases with dehiscence of the wound postoperatively, an incidence of 0.51 per cent. If the 208 inguinal or femoral hernioplasties which were performed during that period are deducted from the total operative procedures, the incidence of wound dehiscence in this series is 0.56 per cent. In spite of the fact that Maes and co-workers[1] have reported a case of eventration following a direct inguinal hernioplasty, which is a comparative rarity encountered in the literature, it would seem that the deduction of hernioplasties provides a truer indication of the occurrence of wound dehiscence.

Mortality.—Maes and others[1] postulate that the most important factors in determining the mortality are the underlying disease process and the physical status of the patient, rather than the wound disruption per se. While this may be true in a considerable number of instances, nevertheless, it cannot be doubted that the occurrence of wound disrup-

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tion quite frequently will transform a fair operative risk with a good prognosis into a seriously ill patient with a poor prognosis.

In the present series of cases there was only one death, or a mortality rate of 7.7 per cent, following wound dehiscence. It is only when we realize that this is an extremely low mortality rate that the full significance of the hazard which wound dehiscence offers to a successful postoperative convalescence becomes apparent. Jenkins[2] in his comprehensive review of the literature found a mortality of 35 per cent in 1,294 cases. Other authors have reported varying rates as follows: Glenn and Moore,[3] 45.4 per cent; Meleney and Howes,[4] 44 per cent; Grace,[5] 39 per cent; Bettman and Lichtenstein,[6] 37.5 per cent; and Koster and Kasman,[7] 17.5 per cent. When we reduce all of the available statistics concerning the incidence and mortality into ordinary figures, we find that approximately 1 patient in every 450 upon whom we perform an abdominal section dies following wound dehiscence.

Sex.—In the present series of cases there was a predominance of the lesions among males, since 9 (69 per cent) of the patients were of that sex. It would be imprudent to conclude on the basis of such a small series of cases that this represents a true incidence in each of the sexes. Jenkins[2] in his review of 1,294 cases also reported a masculine predominance, but to a lesser degree. He reported 57 per cent of the cases in males.

Age Incidence.—Wound eventration has been reported in every age group from infancy to old age. The youngest member in the present series was 22 years of age, while the oldest was 67 years of age. The distribution of cases in the various decades is depicted in Table I. It should not be considered unusual that the greatest number of cases are found in the third, fourth, and fifth decades of life, since it is on this age group that the greatest number of operative procedures are invoked.

TABLE I

AGE INCIDENCE OF WOUND DEHISCENCE

20-30 years inclusive	2 cases
30-40 years inclusive	3 cases
40-50 years inclusive	3 cases
50-60 years inclusive	4 cases
60-70 years inclusive	1 case
	13 cases total

Type of Incision.—The type of incision and its location have been dwelt on by many authors in relation to their liability to or freedom from wound dehiscence. Table II illustrates the various types of incisions and their frequency of dehiscence in the present series of cases. It will be noted that 69 per cent of the cases occurred in upper ab-

dominal incisions. It cannot be construed, however, as indicative of any particular significance that the greatest number of cases occurred in rectus incisions, since this was by far the most frequently utilized type of incision in the 2,318 operations reviewed. The preponderance of upper abdominal dehiscence coincides with the findings of the majority of investigators,[3, 5, 8, 9] but the minority group, as exemplified in the review of a ten-year series at the Charity Hospital in New Orleans, is sufficiently in evidence to prevent any dogmatic statements in this regard.

TABLE II

TYPE OF INCISION THROUGH WHICH DEHISCENCE OCCURRED

Right upper rectus	5 cases	69.1% upper abdominal
Right upper Battle	1 case	
Left upper rectus	1 case	
Upper transverse	1 case	
Upper midline	1 case	
Right lower rectus	2 cases	
Lower midline	2 cases	

It will also be noted that a wound dehiscence in our series of cases occurred following a transverse incision, which is contrary to the findings of several previous authors. Meleney and Howes[4] in their report advocated a greater utilization of the transverse incision because of its freedom from disruption. White[10] stated that in his series of cases disruption had not occurred after intermuscular, Pfannenstiel, costal, or transverse incisions.

In the present series of cases, the only common type of abdominal incision utilized in this hospital which was not complicated by a disruption was the McBurney incision. Colp[11] reasoned that the McBurney incision, on an anatomic basis, should afford protection against dehiscence. Grace[5] substantiated this reasoning in his review of a fifteen-year period on the First Surgical Division at Bellevue Hospital, during which interval there were no disruptions through McBurney incisions. It must not be concluded, however, that this type of incision is impregnable, since a fair-sized series of cases[1] have been reported in which almost 50 per cent of the wound dehiscences followed appendectomies, and in approximately one-third of these cases the McBurney incision was utilized.

Occurrence.—There is probably nothing more appalling to the surgeon following an abdominal laparotomy than to discover an abnormal amount of sanguineous drainage on the dressing after an interval of several days. This phenomenon is an almost constant precursor of wound dehiscence. The drainage in these cases imparts an almost characteristic hue to the dressing which Fraser[12] has aptly described as a "terra cotta" stain. This is not to be confused with the dark glairy appearance of the wound margins following a dehiscence and

is probably due to the reaction in the wound and peritoneum, with a consequent outpouring of serosanguineous exudate.

The presence of profuse drainage, however, is not the only criterion of impending dehiscence which must be heeded in order to anticipate trouble from this source. Lahey[13] cautions, and justly so, that all patients with late or persisting postoperative vomiting or any obstructive symptoms should have their operative wounds carefully examined by the surgeon for any evidences of disruption.

It is well to know what to look for in order to anticipate such dire consequences, but it is also extremely valuable to know at what stage in the postoperative convalescence they may occur. In the present series, ten (77 per cent) cases of dehiscences occurred between the fifth and eighth postoperative days inclusive. The earliest occurrence of this disaster in the group was on the fourth postoperative day, while the latest was on the twelfth postoperative day. These figures approximate very closely the usual time during which disruptions are reported. Jenkins,[2] in his statistical analysis of all the available literature, found that the average time of disruption was 8.3 days postoperatively.

Wound Healing.—Before proceeding farther with a discussion of wound dehiscence, it might be advisable to briefly review the process of healing in a normal uncomplicated wound.

The healing of a wound is far from being a simple, logical train of events. There are many features of the process which are poorly understood and which are highly debatable. In spite of the many theories which are advanced concerning the nature of the process, there are certain definite fundamental facts about which there is almost universal agreement. Since this paper is designed primarily to be a clinical rather than an academic discussion of the subject, an effort will be made to forego debatable issues as much as possible and to present the views which are most commonly accepted.

When an incision is made through a portion of tissue, the amount of trauma and devitalization sustained by its constituent cellular elements is directly dependent upon the precision of the operator and the manner in which the wound is inflicted. A coat of fibrin quickly forms on the incised tissue area. Whether we subscribe to the physicochemical or the physiologic theory on the formation of fibrin is immaterial; the fact that the fibrin is the primary stage in the healing process still remains. If there has been a considerable amount of cellular destruction in the original lesion, the process of phagocytosis will predominate in the initial period, as evidenced by large numbers of leucocytes and mononuclear cells in the substance of the newly formed fibrin. It must not be construed, however, that all other processes are in abeyance. There is a concomitant production of endothelial cells which grow into the architectural framework of the fibrin

from the capillaries of the healthy tissues and give it a cellular structure. The endothelium proliferates to form a vascular tree for the new tissue and from these endothelial elements the cellular structure of the healing wound is derived.

Howes and co-workers[14] have demonstrated experimentally that there is a quiescent phase or "lag period" in the healing of a wound during which its tensile strength per se is zero. This period usually extends for from four to six days. Clark[15] found that this period was susceptible to dietary control and could be reduced by a high protein diet. Harvey and Howes,[16] however, contradict this statement. They maintain that a high protein diet, while responsible for an acceleration in the rate with which the wound heals, does not alter the duration of the initial "lag period." Following the lag period, the tensile strength of the wound rapidly increases until the maximum level is reached in from ten to fourteen days.[14]

A later stage in wound healing, known as the contraction phase, during which there is a compression of the vascularity and an increase in the connective tissue elements, is governed by a variable factor depending on the age of the wound and by a constant factor proportional to the original size. In this phase of a healing wound an increase in dietary protein causes no acceleration and the process proceeds over a period of many months.

Epidermization of a wound is dependent solely on the age of the wound when all other factors are constant. Diet also has no effect on this portion of wound healing.

From this cursory résumé we see that in normal wound healing there is a definite sequence or course which it follows. Probably the most significant aspect in the healing of any wound, so far as the clinical application of the physiologic mechanism is concerned, is the presence of a lag period with its concomitant negligible tensile strength. It is obvious that during this period the wound requires support to maintain coaptation of its margins. It has been for this purpose that suture materials have been a necessary part of the surgical armamentarium since the time of the earliest available records.

Suture Material.—It would appear profitable at this point to consider the various types of suture material available to the surgeon for the purpose of re-enforcing a wound during the period in which it is intrinsically weak. For purposes of discussion we may roughly divide them into two distinct groups: first, absorbable suture material; and second, nonabsorbable suture material.

When one speaks of absorbable suture material, one is referring to a type of material which, when placed in a wound, ultimately will disappear due to the properties of the body tissue in which it is imbedded. Catgut suture is the most common and widely used example of this type of material. It has been prepared in various graded sizes

with initial tensile strengths varying in proportion to the density of the material. Tanning of the gut has been found to decrease its susceptibility to resorption in an uninfected wound, thereby maintaining more closely its initial tensile strength over a longer period of time. Various methods of tanning with a variety of agents have been devised for this purpose, but probably the one having the most universal acceptance in chromicization. Rhoads and his co-workers[17] advocate tanned iodized catgut on the basis of experimental work indicating an average daily decline in tensile strength of less than 50 per cent of medium hard chromic catgut. This view is not held by several of the leading manufacturers of catgut suture material who have discontinued the production of iodized catgut because their research departments revealed such suture material to have a variable absorption rate of iodine as well as an increased perishability due to the destructive action of the iodine on the catgut.

Brewer,[18] in his research for the Council of Pharmacy and Chemistry for the American Medical Association, found that heat-sterilized catgut offered the most consistently bacteria-free suture material when compared with catgut sterilized by chemical methods.

In the present discussion I will avoid reference to ten-day, twenty-day, and forty-day tanned catgut, since it has been showed that at best these are only relative evaluations of the potential life of the suture material when imbedded in tissue under comparatively normal conditions. It will be found more practical to refer to catgut as either tanned or plain, with the understanding that the more highly tanned a portion of gut is the more resistant it will be to resorption. If we wish to formulate these facts more compactly, they may be grouped into two rules: first, the strength of a catgut suture imbedded in tissue varies inversely at a constant rate as a function of time; and second, this rate of variation is directly dependent upon the degree of tanning. These facts are graphically illustrated by the experimental work of Howes and Harvey.[19]

Kraissl[20] calls attention to certain intrinsic factors in the catgut which will increase the rapidity of its dissolution. Since practically all catgut is supplied in tubular ampoules, he has demonstrated that there is a tendency for the gut to fray at the point of bending in the tube. Occasionally foreign bodies incident to its production may be found in the catgut. He also cautions that, due to the necessary dehydration coincident with the production of boilable varieties of catgut, there is a compensatory absorption of fluid by these sutures when placed in tissue, thereby inciting a more vigorous reaction. He also notes that the larger sizes of tanned catgut may be incompletely chromicized due to lack of penetration in the process, consequently lessening their resistance to absorption as well as hastening their absorption due to a larger area on which tissue activity might take place.

Jenkins[2] clinically arrived at the same conclusion when he found that his results were better upon using small sizes of hard, tanned gut.

Thus far we have been concerned with the reaction of catgut sutures which were imbedded in normal tissue. The reaction of catgut in infected tissue is entirely different. It is acknowledged that regardless of the type of catgut which is utilized for wound closure in the presence of infection, it disappears at an abnormally rapid rate. Howes and Harvey[19] state that in an infected wound the intensity of reaction is directly proportional to the degree of chromicization and the amount of catgut imbedded in the tissues. Thus, we see that even the most favorable type of catgut suture material quite frequently may be inadequate in the presence of infection.

Nonabsorbable suture materials present an entirely different array of problems. As their name implies, these suture materials are not resorbed by tissue activity and as a result retain their initial tensile strength after being imbedded in the tissues. Notable among this group of suture materials are silk, silkworm gut, steel alloy wire, silver wire, and several commercially prepared types of suture material. Each type of material has its advocates who voice a preference both for a particular suture and a technique with which it may be utilized.[4, 10, 21-23] There are in general two methods in which these materials may be used: first, closure by layers with the nonabsorbable material permanently located at the site of the closure; and second, closure by a technique whereby the removal of the material from the wound may be accomplished at the termination of the process of healing.

It is an acknowledged fact that, if an infected wound is sutured by layers with a nonabsorbable material which is destined to remain in situ, the results are consistently unsatisfactory. The suture material is a foreign body in the tissues and as such acts as a nidus for the inflammatory tissue reaction, until it is expelled from the wound. This has been frequently demonstrated in the case of silk suture, although any nonabsorbable suture will act in a similar manner. It is obvious that the only indication for the permanent deposition of nonabsorbable suture material in any wound is a case in which there is unquestionably no infection. Glenn and Moore[3] caution in regard to silk suture that even in clean cases there must be no catgut used in the closure lest the tissue reaction excited by the absorbable suture become localized around some of the nonabsorbable type and persist. The limitations of this type of closure are fixed by the type of case. There is always the hazard that should a secondary infection occur in the wound an unsatisfactory termination to the healing of the wound may be anticipated.

The second method of utilizing nonabsorbable suture material is more conservative in its scope and more adaptable to varying condi-

tions which may arise in a wound. Although there are several techniques which utilize removable nonabsorbable suture material for closure by layers, the usual method in which this type of closure is employed consists of the insertion of through-and-through sutures at some distance from the wound margins so as to pass through the depths of the wound. In this manner the wound is supported by suture material of unchanging tensile strength which may be removed after the tensile strength of the wound is sufficient to meet its own needs, thereby eliminating a focal reaction should the wound be infected.

Tissue Strength.—Besides the tensile strength of the material which is utilized in a wound closure, another important factor must be taken into consideration; namely, the holding power of the tissue in which the suture is placed. When sutures are inserted in a tissue under tension, they produce definite changes in the tissue which eventually may result in a weakening of the suture line. Gratz[24] has pointed out that such weakening will vary directly with the elasticity of the tissues in which the sutures are placed. Elasticity is defined as that property which causes a body to resist deformation and afterwards recover its original size and shape. He found that connective tissues in the human maintain their elasticity when subjected to a stress parallel to the direction of their fibers to a minimal tensile strength of 7,100 pounds per square inch. When the stress is not parallel to the direction of the fibers, however, the shear phenomenon takes place and the minimal tensile strength is decreased. Howes and Harvey[19] found that the initial holding power of a stitch diminished by 50 per cent in the first two days and then remained constant until after the fourth day, when the healing strength of the wound overshadowed the strength of the stitch. They also demonstrated that only in fascia and similarly condensed layers of connective tissue is the holding power of the stitch greater than the tensile strength of the finest catgut. From these facts it would appear obvious that the keystone of adequate wound closure is fascial approximation. The tension on fascial tissue must be distributed in such a manner as to remain well within the minimal limits of stress for the area of tissue involved. In other words, the potential stress to which the suture line may be subjected must be borne by a sufficient amount of fascial tissue at the time of the wound closure if the incision is to be expected to remain intact.

Etiology.—In view of the facts which have been enumerated concerning normal wound healing, suture materials, and the holding power of tissues, it would be well at this point to consider their relationship with the etiology of wound disruption, and, more particularly, with the disruption of abdominal wounds.

Freeman[25] advanced an explanation for wound disruption on the basis of an inadequate peritoneal closure. He postulated that a tag

of omentum is allowed to insinuate itself between the cut edges of peritoneum and act as an expansile wedge due to its subsequent strangulation and engorgement. Several other authors[23, 26] have subscribed to this explanation. In view of the fact that the peritoneum has little tensile strength and that the brunt of the burden for maintaining coaptation between the wound margins is borne by fascial structures, this explanation accounts for the disruption of only the peritoneal layer.

Von Graff[27] propounded the view that wound disruption is dependent upon obesity and diabetes, or at least disturbed carbohydrate metabolism. The relative infrequency with which obesity and diabetes as a group are attended by wound disruption would tend to make this hypothesis very insecure, if not entirely untenable.

The culpability of incomplete anesthetic relaxation was stressed by Heyd[28] as a contributory cause to wound dehiscence. The presentation, however, of a series of seventeen cases of disruption by Koster and Kasman[7] with an incidence of 0.22 per cent under the perfect relaxation afforded by spinal anesthesia seriously detracts from this position.

During the past several years, allergy has been indicted, notably by Babcock,[21] Kraissl,[20] and Hinton,[29] as a potent factor in the causation of dehiscence. They maintain that some individuals, particularly those who have had a previous operation and have an allergic diathesis, may develop a sensitivity to catgut, chromic gut, or chromic acid salts. This sensitivity initiates an unfavorable wound reaction culminating in disruption when these materials are utilized in the repair of an operative wound. This theory, however, fails to explain those occurrences, such as three in the present series of cases which were repaired with a nonabsorbable suture material and which disrupted. Another point which vitiates the potency of this factor in wound dehiscence is the experimental work by Frugoni,[30] in which he demonstrated that due to its intrinsic character, being composed of albumoses rather than albumens, catgut has a relatively weak or negligible antigenic potency, although his work does not establish this point conclusively.

Hypoproteinemia has been advanced by several authors[31, 32] as a contributory factor to wound dehiscence in a certain small percentage of cases. It has been shown that in the presence of a protein deficiency there is a retardation in the rate of wound healing together with an accentuated decline in the tensile strength of the catgut supporting the wound. This has been corroborated by both experimental and clinical research, but it is advanced merely as a contributory factor. The dehiscence in these cases results per se because the material coapting the imperfectly healed wound margins withdraws its support before the tensile strength of the wound is sufficient to maintain this function.

Increased intra-abdominal pressure, incident to retching, coughing, straining, or distention, has been the most frequently indicted factor in the cause of wound dehiscence.[8, 9, 33] Although several authors[1, 6] attach little significance to this etiology, owing to its relative frequency in any series of postoperative cases, nevertheless, its consistent occurrence in this complication cannot be justly disregarded. In the present series of thirteen cases, twelve had either cough or distention of an appreciable nature prior to the occurrence of wound dehiscence. The error has been made once again of attributing to the increased intra-abdominal pressure the causation of the dehiscence rather than allotting to it the contributory role which it justly deserved.

The crux of the etiology of wound dehiscence lies in the definition of the purpose for which suture material is used in a wound. The function of suture material is to maintain tissue apposition until the process of wound healing has progressed to such a degree that the tensile strength of the wound is sufficient to render such artificial support unnecessary. The surgeon, when repairing such a wound, must take into consideration all the factors which may be functioning during the interim before the wound itself acquires sufficient tensile strength, and he must provide measures to compensate for them. The solution of this problem will be arrived at only when a definite technique of wound closure is utilized which can fulfill all of these requirements. Whether a case develops a wound infection, an increased intra-abdominal pressure, wound allergy, or a state of hypoproteinemia postoperatively, the initial closure should have been such as to meet any stress which these conditions might impose.

Prophylaxis.—The elimination of postoperative wound dehiscence is entirely within the jurisdiction of the operating surgeon. It is no longer an abstruse complication for the investigation of the research laboratory. The question of whether the incidence of this distressing complication will be ultimately abolished rests in the hands of the clinician. The first approach to the solution necessarily will be a better understanding of wound healing, suture materials, holding power of tissues, and the action of the various conditions which may arise postoperatively in the wound. The fact that Baldwin,[34] utilizing a definite technique in closure, has been able to report a series of 16,465 abdominal sections without dehiscence offers clinical proof that the abolition of wound dehiscence is not a mere surgical Utopia. Kennedy's[35] report of not a single dehiscence during a period of thirty-six years at the Joseph Price Hospital, where an equally adequate but dissimilar technique was utilized, serves as added emphasis.

Undoubtedly, catgut suture will continue to remain the predominant medium utilized in wound closure. The adequate perception of the physiologic mechanism in wound healing together with an understanding of the decline in tensile strength of absorbable suture material

undoubtedly will result in the greater utilization of smaller sizes of tanned catgut in a meticulous manner; i.e., interrupted sutures with small tissue bites, such as is advocated for the use of nonabsorbable suture material destined to remain in situ. The unvarying tensile strength of nonabsorbable suture in a wound closure, however, will be a necessary prerequisite if we are to contend successfully with the various factors, such as infection, allergy, and hypoproteinemia, which may vitiate the stability of an absorbable suture closure. Moreover, these nonabsorbable sutures, whether they be silkworm gut, silk, silver wire, or steel alloy wire, must be placed in such a manner as to maintain an adequate coaptation and holding power in the tissues should an abnormal strain be placed on the suture line due to increased intra-abdominal tension. The easiest and most practicable manner in which this can be accomplished is by through-and-through sutures placed sufficiently near each other so as to distribute their tension on the fascial structures evenly and through a wide area. It would appear, on the basis of the present evidences, that the ideal closure of abdominal wounds consists in careful tissue approximation by fine catgut sutures re-enforced by an adequate number of nonabsorbable retention sutures which have been placed through all the layers at an optimum distance from the wound margins to insure their holding power.

CONCLUSION

In the present article a series of 13 cases of wound dehiscence is reviewed. The more rational utilization of both absorbable and nonabsorbable suture materials is advocated in keeping with the known facts concerning wound healing, suture tensile strength, tissue-holding power, and the factors influencing wound dehiscence.

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THE USE OF SULFANILAMIDE IN SURGERY OF THE COLON AND RECTUM

Preliminary Report

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THE importance of postoperative peritonitis, retroperitoneal phlegmon, and extensive wound infections in surgery of the large bowel is fully realized. Analysis of the causes of death in published statistics from this and other countries indicates that peritonitis heads the list. The advances in the surgery of the colon and rectum in recent years have been in two directions. First, it has become increasingly evident that graded multiple-stage procedures are more desirable from all standpoints. The consensus of opinion seems to be that this point of view admits of little argument. Second, attempts have been made to develop some method which would vaccinate the peritoneum against infection. There is no need of an extended discussion of this phase of the subject at this time. Suffice it to say that neither the mixed vaccine recommended by Bargen and Rankin, amniotin, nor any of the other recommended substances has produced the peritoneal immunity hoped for by their various proponents. Only recently, Rankin voiced his disappointment with the results of an extensive experience with the mixed vaccine of streptococci and *B. coli*.

About a year ago this study, the results of which are briefly reported herewith, was undertaken in the hope of throwing some light on the problem of postoperative peritonitis.

The work has been conducted by one of us (G. P. S.) in the Department of Bacteriology under the direction of Dr. Gregory Schwartzman, to whom we are indebted for invaluable advice and suggestions. Briefly, the plan of procedure consisted of: (1) the taking of cultures at the time of operation from the retroperitoneal and pericolonic tissues, especially in the vicinity of the carcinoma; (2) under aseptic precautions, the bowel wall was incised in the region of the growth and cultures were made from all layers; and finally (3) cultures were made from the mucosal surface of the neoplasm. Both aerobic and anaerobic preparations were made in each instance. A more detailed report of this study will be made by one of us (G. P. S.) in the near future.

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This study, which was started in January, 1938, soon showed that the predominating organism was a hemolytic streptococcus, associated in most instances with *B. coli*. On the basis of these findings, one of us (J. H. G.) suggested the use of sulfanilamide preoperatively as a prophylactic measure. The routine preoperative administration of sulfanilamide in all cases of small and large bowel surgery was started in March, 1938. Since that time, in a group of 21 consecutive cases that have been subjected to operation and cultured according to the plan above described, there has not been one positive culture of *Streptococcus hemolyticus* in either the retroperitoneal tissues, the bowel wall, or the mucosal surface of the neoplasms. The organisms demonstrated in these 21 cases may be tabulated as shown in Table I.

TABLE I

B. coli alone	2 cases
B. coli, *B. welchii*, enterococcus	3 cases
B. coli, enterococcus	10 cases
B. coli, *B. subtilis*, enterococcus	3 cases
B. coli, *B. pyocyaneous*, enterococcus	1 case
B. coli, enterococcus, *Staphylococcus aureus*	1 case
No growth	1 case

These 21 cases included the conditions given in Table II.

TABLE II

1. Abdominoperineal resection for carcinoma of rectum and rectosigmoid in one stage	5 cases
2. Obstructive resection for carcinoma of transverse, splenic flexure, descending and sigmoid colon	7 cases
3. Carcinoma of cecum	1 case
4. Colectomy for ulcerative colitis	2 cases
5. Two-stage Lahey operation for carcinoma of rectum	3 cases
6. Subtotal colectomy for multiple polyposis with carcinoma of sigmoid	1 case
7. Fibrosarcoma of ileum	1 case
8. Obstructive resection for acute suppurative sigmoiditis	1 case

In this group of 21 cases there were 2 deaths. One patient who had an obstructive resection for carcinoma of the splenic flexure experienced an uneventful convalescence until the seventh day when he suddenly went into collapse and died within five minutes. The clinical picture suggested either a pulmonary embolism or a coronary artery occlusion. There was no post-mortem examination. The second patient had an abdominoperineal resection for carcinoma of the rectum in one stage. His postoperative course was uneventful until the fifth day when he developed pulmonary edema quite suddenly. The clinical picture suggested coronary artery disease. Death occurred within six hours and at autopsy there was found a fulminating tracheobronchitis and bronchopneumonia which the pathologist, Dr. Paul Klemperer, con-

sidered to be of the influenzal type. The peritoneal cavity was perfectly clean, as was also the perineal wound. The colostomy had been functioning properly.

The analysis of wound healing in these cases is of considerable interest. In only one instance was there a major wound infection and it was expected in this particular case. This patient had an obstructive resection for a perforated carcinoma of the sigmoid with a perisigmoidal abscess, and gross soiling of the wound and adjacent peritoneum occurred during the manipulations incident to freeing of the bowel. *B. coli* was recovered from the wound. Yet, in spite of this serious accident, convalescence was remarkably smooth. Another case of obstructive resection of the sigmoid developed a small stitch abscess. A third patient developed a mild infection of the posterior wound following an abdominoperineal operation.

In two cases of abdominoperineal resection for carcinoma of the rectum, the rectum was accidentally opened during the perineal part of the operation and gross spilling occurred. Yet, no infection developed and convalescence was uninterrupted. Finally, one of our most recent cases is of considerable interest. This patient, a woman 54 years of age, had a carcinoma of the rectum with considerable fixation to the posterior vaginal wall. Because of this, a two-stage Lahey operation was decided upon. During the course of the second stage, an abscess between the tumor and the vaginal wall was entered into and gross soiling of the peritoneum occurred. The operation was continued and a new pelvic peritoneal diaphragm was reconstructed. Except for a temporary mental upset attributed to the spinal anesthesia, convalescence was not marred in the slightest by this accident. There was no infection of either the anterior or posterior wounds. *B. coli* was cultured at the time of operation.

We have been impressed with the smooth uncomplicated convalescence of these patients, in spite of the fact that there have been no changes in operative technique. On this service, the one-stage Miles operation is usually employed for carcinoma of the rectum. Occasionally a two-stage procedure is decided upon for one reason or another. For neoplasms involving the transverse and left half of the colon, obstructive resections usually are performed. For carcinoma of the cecum and ascending colon, resection in one or two stages is done, depending upon the age and general condition of the patient. We have been using the so-called open type of anastomosis routinely. The improvement in postoperative morbidity and mortality, therefore, cannot be ascribed to any change in choice of operation or operative technique.

Before routine preoperative administration of sulfanilamide was instituted, cultures were made in six cases according to the method above described. These included 4 abdominoperineal resections in one

stage, one Lahey procedure, and one obstructive resection for carcinoma of the transverse colon. In 4 instances the cultures revealed hemolytic streptococcus in association with *B. coli*. One case showed *B. coli* and an anhemolytic streptococcus, and the sixth cultured *B. coli* alone. In this group of 6 patients there were 2 major abdominal wound infections and 1 posterior wound infection.

Our routine preoperative preparation includes, in addition to a low-residue diet, glucose, transfusions when necessary, etc., the administration of sulfanilamide by mouth for three days before operation in 15 gr. doses every four hours day and night. We attempt to keep the sulfanilamide blood concentration between 5 and 6. Daily blood counts are done. It is important to watch closely for evidences of sulfanilamide intoxication. Many of the patients have developed the peculiar cyanosis frequently seen following the administration of this drug. In most instances, use of the drug is continued postoperatively for two or three days. No untoward results have been noted to date.

In order to amplify further the bacteriologic investigation, the results of which we have briefly reported in this paper, a change in procedure has been instituted. At the present time, every patient with a carcinoma of the rectum or rectosigmoid is sigmoidoscoped following a cleansing enema and cultures are made from the surface of the tumor, before sulfanilamide therapy is instituted. The results of these cultures will be compared with those taken at the time of operation. It is hoped that additional light will be thrown on the subject by these investigations. This phase of the work will be reported in detail by one of us (G. P. S.).

We have indicated in this preliminary report our experiences with the routine preoperative administration of sulfanilamide in surgery of the colon and rectum. It seems, after a careful evaluation of the clinical course of this group of patients, that the postoperative phase has been singularly uncomplicated, the morbidity has been unusually slight, and peritonitis has been nonexistent. In this connection it is important to note that, in 21 consecutive cases, *Streptococcus hemolyticus* was not recovered in any of the cultures made. It is realized that the number of cases reported herewith is not sufficient to warrant definite conclusions. However, the impression gained is that the results obtained so far warrant a continuation and extension of this study.

Editorial

Fascia in Surgery

DURING the last fifteen years there has been a marked increase in the use of fascia in surgical conditions of all sorts. This applies to both sheets and strips of fascia, and to both autogenous and preserved. Fascia strips have been used as suture material in various conditions, to replace tendons and ligaments, and to hold various organs in position, or to fix certain parts that have lost their normal function, either through paralysis or operative accidents. Sheets of fascia have been used to repair fascial defects in various places, to reinforce suture lines, to furnish fascial bands for various purposes, and to keep raw surfaces apart, as in arthroplasty.

Fascia strips have been used as suture material more often in hernias than in other conditions. Indeed, it was the work of Gallie and LeMesurier on their "living sutures," a little more than fifteen years ago, that brought the use of fascia strips into such prominence. The strips have been used in the repair of hernias of all kinds, inguinal, femoral, umbilical, and postoperative. Some surgeons have gone so far as to use them as a routine procedure, while others use them only in their most difficult cases. There is a pretty general consensus of opinion that better results are obtained in difficult hernias when fascia strips are used than when other suture materials are used. However, a few surgeons deny this, claiming that the important thing is a correct apposition of the parts and that the type of suture material is a less important matter. It seems to me that both are important.

Among other uses of fascia strips as suture material might be mentioned their use in fractures, such as fractures of the olecranon and of the patella. They have been used successfully also in suture of acromioclavicular separation. They have been used also to suture defects due to spina bifida, to suture muscles to tendons, and to repair joint capsules, especially in the operation for habitual dislocation of the shoulder.

Fascia strips have been used to replace parts, or to fix parts, as follows: To replace the crucial ligaments of the knee; to supply tendon defects; to suspend the vault of the vagina when the uterus and round ligaments have previously been removed; to fix the corner of the mouth in facial paralysis; in congenital ptosis of the upper eyelid; and in the operation for complete incontinence of feces, using double bands around the anus and through the gluteus maximus muscles on each side, thus establishing voluntary control.

Sheets of fascia have been used to close hernial defects, the edges of which cannot be approximated, often strips of fascia being used to

suture in the sheets. They have also been used to strengthen suture lines after hernial defects have been repaired under some tension, or when the structures used in making the repair have been weak. Sheets also have been used to repair dural defects, in arthroplasties, and to make cylinders to bridge tendon defects. Bands of fascia have been used to replace annular ligaments, to hold fractures in apposition, and around the aorta in cases of aneurysm.

Both autogenous and preserved (ox fascia) fascia have been used in almost all the conditions mentioned above. In our experience, both experimental and clinical, one is found to work as well as the other.

The results reported from various parts of the country in the use of fascia, especially in its use for hernia repair, have been somewhat inconstant, both with regard to autogenous fascia and ox fascia, but more specially with regard to the latter. It is quite probable that in those cases in which poor results have been obtained, the fault has been due to technical errors of various sorts. For a time bad results were obtained when ox fascia were used, due to a manufacturer's error in putting the strips up in an irritating solution. That error has long ago been corrected, and the strips are now put up in 1 per cent biniodide of mercury in alcohol. This is necessary to insure sterilization, as the strips cannot be taken out of oxen in slaughter houses in an aseptic manner. However, before ox fascia strips are used, all of the preserving fluid should first be washed out carefully in salt solution, otherwise there will be some chemical irritation in the wound as a result. The strips should be washed thoroughly in one basin of salt solution and then rinsed in another. It is the practice of some surgeons to let them soak for a couple of hours before using them. The point of thoroughly washing the strips in salt solution before they are used, has been mentioned before, but I believe has not been sufficiently stressed. It is a very important point and upon it depends satisfactory results in the use of ox fascia strips. Once the strips are free of any trace of chemical, they are entirely nonirritating, and the collagen fibrils in them differ in no way from those of autogenous fascia. In either case, the collagen fibrils simply act as a framework for the ingrowth of fibroblasts and blood vessels from the tissues of the host, because in the case of autogenous fascia grafts the cells between the fibrils die and have to be replaced.

It is often stated that autogenous fascia plays an active part in repair while preserved fascia plays a passive part. That this is an erroneous view is obvious from what has just been said about the manner of "taking" of both implants. The mechanism is the same in the one as in the other.

In the use of fascia, as in the use of any other surgical procedure, attention to technical details is a matter of great importance. Fascia has no magical qualities and its use in a sloppy manner will give results just as poor as, or poorer than, if it had not been used at all. Among the

technical details that should be stressed is the testing of the strength of fascia strips before they are used. If fascia is cut on a bias, it has no tensile strength and will pull in two. Fat and excess areolar tissue could be carefully cleaned off. The presence of areolar tissue tends to produce a flimsy type of union instead of the firm type which ensues when the fascia is opposed to fascia without an intervening layer of areolar tissue. If one end of the strip is smaller than the other, the small end should be put in the needle and the larger end left free for anchoring. Care should be taken also to see that the anchoring is made in firm tissue and that all areolar tissue is cleared off from the area to be sutured before the suturing is started. In putting a needle through a fascia strip in anchoring, in splicing, or in putting in lock stitches, care should be exercised to see that the needle pierces the strip exactly in the center, else there is danger of tearing the strip. The ends of the fascia strips should be tied off with silk, linen, or steel wire, and not with some absorbable material. This, of course, also applies to suturing the strip in the needle. It is absolutely essential that the fascia strips stay in place long enough to ensure firm healing. If absorbable material is used to tie off the ends of the strips or to suture them into the needle, this is very likely to give way in a few days, as considerable tension is put upon it. If one such transfixion ligature gives way, the whole fabric of the repair is loosened. Likewise, it is essential that the final end of the suture line be firmly anchored in some appropriate manner, either by splitting the strip and tying, or by suturing the end firmly into some fascial structure with a nonabsorbable suture material. Since nonabsorbable suture materials are used, as just described, they should be used throughout the operation, both for ligatures and for other sutures, as it has been shown definitely that catgut and nonabsorbable sutures should not be used in the same wound. Use either all of one or all of the other. Infection supervenes much more often when they are mixed.

Finally it has been pointed out by a number of authors that infection does not necessarily vitiate the results in cases where fascia is used. Naturally, one would not expect the result to be as good in infected cases and infection necessarily results in some failures. However, many infected cases get excellent results and in the presence of gross infections, it is remarkable how little of the fascia sloughs out. In most cases only small pieces of fascia, a few millimeters square, are lost. In one case in which a large piece of ox fascia was used to repair a postoperative hernial defect, in which the edges of the defect could not be approximated, eventually two or three pieces of ox fascia strip, each about an inch long, that had been used to suture in the sheet of fascia came out. However, the sheet remained in place, and the result was a cure of the hernia.

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

THE RELATION OF VITAMIN K TO THE HEMORRHAGIC TENDENCY IN OBSTRUCTIVE JAUNDICE, WITH A REPORT ON CEROPHYL AS A SOURCE OF VITAMIN K

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VITAMIN K was discovered by Dam in 1934[19] as a new accessory food factor required for the normal development of chicks. Since withdrawal of the vitamin from the diet of the common laboratory mammals produced no symptoms, the attention of physicians was not directed to it until 1938 when three separate groups of investigators[15, 22, 81] showed that it could be successfully used to combat the hemorrhagic tendency in obstructive jaundice.

It now appears that this entity, which has puzzled physicians and surgeons so long, is merely another conditioned deficiency, a deficiency of vitamin K conditioned by the absence of bile salts from the intestinal tract. In the absence of bile salts vitamin K is not absorbed in adequate amounts from the intestine.

It is impossible to review the discovery and development of vitamin K without simultaneously considering some of the work on the hemorrhagic tendency in jaundice. This subject has been developed in two directions. On the one hand, attempts have been made to devise a test to detect the hemorrhagic tendency preoperatively. Bleeding time, clotting time, serum calcium concentration, fibrinogen concentration, prothrombin time by the method of Howell,[43] and sedimentation rate as recommended by Linton[50] were tried and found unreliable. The Ivy bleeding time,[44] the clotting index of Bancroft, Kugelmass, and Stanley-Brown,[11] and the clot volume index of Boyce and McFetridge[12] were proposed later and are still being tried.

On the other hand, attempts were made to treat the hemorrhagic tendency both prophylactically and therapeutically. Calcium was given by mouth and intravenously, high carbohydrate diets and intravenous glucose therapy were recommended, and pre- and postoperative transfusions were tried. This subject was reviewed by Ravdin and Johnston[64] and by Ivy, Shapiro, and Melnick.[45] An evaluation of

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the methods of treatment employed at the Hospital of the University of Pennsylvania in a series of 155 cases was reported by Ravdin and co-workers.[66] Both the need for a prognostic test and the need for effective methods of treatment have been met since by the discovery of the relation of vitamin K and prothrombin to the hemorrhagic tendency in obstructive jaundice.

PROTHROMBIN

In 1935 Quick[57] introduced a new method for determining prothrombin in plasma. He observed that the Howell[43] prothrombin method was relatively insensitive to dilution of the plasma specimen. The two most widely accepted theories of blood coagulation, that of Morawitz[54] and that of Howell,[43] agreed on four necessary constituents for clot formation: prothrombin, thromboplastin, calcium, and fibrinogen. The presence of an optimum amount of fibrinogen has been demonstrated to be constant except after total hepatectomy or in the terminal stages of liver injury.[35, 51] In the Howell method an optimum amount of calcium was added, but two variables, prothrombin and thromboplastin, remained. Quick[57] showed that by the addition of an excess of thromboplastin in the form of suitable tissue extracts the prothrombin time could be reduced to a fraction of the figure obtained by the older method. He developed a test for prothrombin suitable for the clinical laboratory which depended on the addition of a rabbit brain emulsion to oxalated plasma before recalcification.

Using this method Quick, Stanley-Brown, and Bancroft[62] were able to demonstrate a prothrombin deficiency in a number of jaundiced patients and stated that this deficiency was the cause of the hemorrhagic tendency. Quick has since modified the test several times but the principle has not been changed.[58, 61*]

A test for coagulability similar to Quick's method for prothrombin has been employed by Schønheyder[70] and by Dam and Glavind[25] based on a method of Fischer.[34] According to this method, instead of determining the time of coagulation of the unknown plasma, one compares the concentration of the thromboplastin preparation required to clot

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*Attention is called to what the author believes are typographical errors in the descriptions of two of Quick's methods.

With the method described in the paper entitled "A Study of the Coagulation Defect in Hemophilia and in Jaundice" by Quick, Stanley-Brown, and Bancroft in the *American Journal of the Medical Sciences* **190**: 501, 1935, more satisfactory results have been obtained if 0.2 gm. of the dried rabbit brain is emulsified in 3 c.c. of physiologic saline solution instead of 0.3 c.c.; and in the paper entitled "The Nature of the Bleeding in Jaundice"[61] more satisfactory results have been obtained if fortieth molar calcium chloride solution is employed for recalcification than with tenth molar as directed in the paper.

We prefer the method of thromboplastin preparation described in 1936[58] to the later method employing acetone extraction,[61] because of the greater stability of the resulting product.

For sources of error in prothrombin determination, Aggeler, P. M., and Lucia, S. P.: Proc. Soc. Exper. Biol. & Med. **39**: 11, 1938; and Stewart, J. K., and Pohle, F. J.: Ibid. **38**: 532, 1938, should be consulted.

the unknown plasma in a standard time interval with the concentration required to clot normal plasma in the same interval.

Probably the most accurate test for prothrombin is that of Warner, Brinkhous, and Smith.[82] In this procedure the prothrombin is first converted quantitatively to thrombin and the concentration of the resulting material required to clot a fibrinogen solution in a standard time interval determined. These authors also investigated the influence of antithrombin and showed that it was not an important factor in the hemorrhagic tendency in jaundice. It should be emphasized that all of these methods depend on the addition of thromboplastin.

Brinkhous, Smith, and Warner[14, 81] demonstrated a prothrombin deficiency in certain jaundiced patients and Dam and Glavind[22, 25] corroborated this finding. The percentage of jaundiced patients who bleed is not great, but the evidence that those who do bleed have a diminished prothrombin concentration is rather convincing (Table I).

There is general agreement that normal blood contains an excess of prothrombin. Quick[61] states that no serious bleeding is observed from prothrombin deficiency until its concentration sinks to below 10 per cent of normal. Brinkhous, Smith, and Warner[14] cite one case that exhibited a hemorrhagic tendency with a prothrombin concentration of 34 per cent. Little change is found in the coagulation time by the usual methods until prothrombin concentration has fallen to 15 per cent of normal.[61]

Quick[61] states that relatively few jaundiced patients have a reduced prothrombin concentration. In 43 patients with obstructive jaundice whose plasma was studied in the Harrison Department of Surgical Research the prothrombin time was significantly prolonged in over 40 per cent.

A reduction in the prothrombin concentration may also occur in patients with external biliary fistulas as demonstrated by Brinkhous, Smith, and Warner.[14] Hemorrhagic phenomena in a patient with this condition were previously described by Judd, Snell, and Hoerner[47] and a similar case was encountered by Ravdin.[63]

VITAMIN K

Vitamin K, which was discovered by Dam[17, 19] while studying sterol metabolism in chicks, is a fat-soluble vitamin. Dam found it in the non-sterol easily saponifiable fraction of hog liver fat. It is readily soluble in ether, hexane, and hot methyl alcohol (50° C.). It may be precipitated from the latter solvent by chilling. It vaporizes between 120° and 145° C. in vacuo. Its chemical characteristics have been investigated by Dam and his co-workers[20, 29] and very extensive studies have been carried out by Almquist[1, 2, 4, 5] and by Klose, Almquist, and Mecchi.[48]

TABLE I

PROTHROMBIN ESTIMATIONS OF PLASMA FROM PATIENTS WITH OBSTRUCTIVE JAUNDICE WHEN THEY HAD HEMORRHAGIC PHENOMENA

AUTHOR	DIAGNOSIS	PROTHROMBIN PER CENT OF NORMAL	PROTHROMBIN TIME (QUICK) (SECONDS)	COAGULATION TEST OF DAM AND GLAVIND
Brinkhous, Smith, and Warner	1. Carcinoma of pancreas	37		
	2. Cholangitis; abscess of head of pancreas	23		
	3. Cholangitis?	34		
	4. Carcinoma of pancreas	17		
	5. Common duct stones	16		
	6. Carcinoma of biliary tract	10		
Dam and Glavind	7. Carcinoma			Decreased coagulability
	8. Cholelithiasis			(same)
	9. Cholelithiasis			Normal coagulability
Quick	10. Common duct obstruction due to an adhesion	2.5		
Butt, Snell, and Osterberg	11. Carcinoma head of pancreas		95	
	12. Carcinoma head of pancreas		170	
	13. Carcinoma common duct		105	
	14. Carcinoma hepatic duct		75	
	15. Stricture of common duct		70	
	16. Carcinoma head of pancreas		60	
	17. Cirrhosis of liver		48	
	18. Carcinoma head of pancreas		180	

Dam and Lewis[27] concentrated vitamin K 1,100 times from dried alfalfa and Almquist obtained it as a crystalloid.[3] Osterberg[55] has described a method of concentrating it from fish meal. Thayer, MacCorquodale, Binkley, and Doisy[74] report obtaining it in crystalline form. The melting point of the crystals is 69° C. Its chemical composition has not been reported.

The discovery of the vitamin followed independent investigations of a hemorrhagic disease of chicks by Dam in Denmark and Almquist in this country. On certain diets adequately supplied with other vitamins, chicks develop hemorrhages into subcutaneous tissues, skeletal muscles, and the gizzard. This phenomenon was noted by Dam[17, 18] in 1929, by McFarlane, Graham, and Richardson[53] and McFarlane, Graham, and Hall[52] in 1931, and by Holst and Halbrook[42] in 1933. That the disease was caused by the lack of a new accessory food factor was recognized by Dam,[19] Dam and Schønheyder,[28] and Almquist and Stokstad.[7] The designation K (Koagulations) was suggested by Dam.[20, 21]

The distribution of the vitamin was studied by Dam[20, 23] and by Almquist[7-9] and their co-workers. Hog liver fat, putrified fish meal, alfalfa, kale, spinach, and hemp seed were found to be excellent sources. Egg yolk is a fair source, especially if the laying hen has been given a diet rich in vitamin K.[8] Cod liver oil, unpolished rice, wheat germ oil, lemon juice, and yeast were poor sources.

Dam and Glavind[23] showed that the vitamin was abundant in peas germinated in the light but not in those germinated in the dark and showed that there was little deterioration of the K content of leaves upon withering.

The presence of the vitamin in the feces of animals was shown by Almquist and Stokstad,[8] and Dam and Glavind[22] report its presence in the feces of man after seven days on a K-free diet. Almquist, Pentler, and Mecchi[6] showed that several common bacteria appear to contain the vitamin even when grown on K-free media. Among these are the colon bacillus and the *Staphylococcus aureus*. Diets free of vitamin K have been described by Dam[19, 21, 28] and by Almquist and Stokstad.[7, 8] Almquist diets have been used in most of the work in this country.

Methods of assay have been developed by Dam,[21] Dam and Schønheyder,[29] Dam and Glavind,[24] Almquist and Stokstad,[7] Thayer, McKee, MacCorquodale, and Doisy,[75] Ansbacher,[10] and Dann.[32] Both preventive and curative methods have been employed. Thus far all assays have been carried out on chicks.

Dam has employed a unit defined as the least amount of vitamin K per gram of chick per day capable of producing normal coagulability in the blood of a K-avitaminotic chick after three days' feeding[70] and has used a dried spinach preparation as a standard.[22]

The cause of the hemorrhagic disease which develops in K-avitaminotic chicks was studied by Dam, Schønheyder, and Tage-Hansen.[31] They reported a coagulation defect due to a lack of prothrombin and showed that this factor returned to normal after the administration of foods which were rich in vitamin K. This finding was confirmed in this country by Quick,[59] who studied chicks given an Almquist diet. Thayer, McKee, MacCorquodale, and Doisy[76] suggested that the vitamin K may have a specific effect in curing the anemia of K-avitaminotic chicks apart from the fact that the loss of blood is stopped. This is denied by Almquist;[9] the evidence does not appear certain.

Attempts to produce hemorrhagic phenomena in other species by diet have been only partially successful.[30] The duckling and the gosling developed the disease. Pigeons and canaries showed some evidences of it, but it could not be produced in rats,* guinea pigs, or dogs by dietary means alone. A mild K-avitaminosis was developed

*J. D. Greaves since has reported producing a K deficiency in 12 of 77 rats by a K deficient diet (Am. J. Physiol. 125: 429, 1939).

by Dam and Glavind[25] in one rabbit. The deficiency was relieved by administration of K and produced a second time.

The intravenous injection of concentrated preparations of the vitamin into K-avitaminotic chicks was reported by Dam, and co-workers[26] who were able to restore the coagulability of the blood to normal in five hours, and later by Ansbacher,[10] who was able to restore the prothrombin concentration of the chicks' plasma to normal levels in two and one-quarter hours. Intramuscular injection was effective, but a longer period was required.[26]

Before vitamin K was successfully used in the treatment of prothrombin deficiency in the jaundiced patient, considerable experimental data on the relation of abnormalities of the biliary tract to blood coagulation had accumulated which served as an important guide to the clinical application of the vitamin. In 1935 Hawkins and Whipple[41] produced hemorrhagic phenomena in dogs by complete biliary fistulas. Hawkins and Brinkhous[40] showed that those hemorrhagic phenomena were due to a prothrombin deficiency using the technique of Warner, Brinkhous, and Smith.[82] Quick[60] suggested that the lack of bile salts in the intestine might interfere with the absorption of vitamin K. Greaves and Schmidt[38] produced prothrombin deficiency in the rat by bile fistulas and by ligation of the common duct. They further demonstrated that the deficiency could be corrected by giving enormous doses of vitamin K or by giving small doses of the vitamin along with bile salts.

Vitamin K, like vitamin D, is a fat-soluble material and is in turn dissolved by fat solvents. It had previously been shown by Greaves and Schmidt[39] that vitamin D was poorly absorbed in the absence of bile salts and their later paper[38] made it apparent that bile salts played a major role in the absorption of vitamin K.

Smith, Warner, Brinkhous, and Seegers[72] demonstrated that the prothrombin deficiency in bile fistula dogs could be relieved by the administration of alfalfa and bile salts. This explains the success of Judd[46] and Wangensteen[79] in preparing jaundiced patients for operation by feeding bile preoperatively, a method to which too little attention was given. Recently animal bile desiccated in vacuo has been used by Johnston[44] and Winfield[83] preoperatively in certain biliary tract cases.

Clinical success in treating jaundiced patients who showed a prothrombin deficiency by the oral administration of vitamin K and bile salts was reported by Warner, Brinkhous, and Smith[81] and by Butt, Snell, and Osterberg,[15] from the Mayo Clinic.

Intramuscular administration of K concentrates has been employed successfully in patients by Dam and Glavind[22] and by Butt, Snell, and Osterberg[16] at the Mayo Clinic. These latter authors found the method inferior to the oral method of administration which they

employed.[15] They demonstrated that the oral administration of vitamin K without bile salt did not increase the prothrombin concentration in a case of obstructive jaundice but that a slow increase could be obtained in a patient with this condition by the administration of normal bile with a normal diet.[15]

More detailed reports on the clinical use of vitamin K have been published by Brinkhous, Smith, and Warner[14] and by Snell, Butt, and Osterberg.[16, 73] The material used and the results obtained are summarized in Table II.

TABLE II

REPORTED INSTANCES OF THE TREATMENT OF PROTHROMBIN DEFICIENCY IN JAUNDICED PATIENTS WITH VITAMIN K AND BILE SALTS

AUTHORS	NO. OF PATIENTS	SOURCE OF VITAMIN K	BILE SALT	RESULTS
Warner, Brinkhous, and Smith[81] Brinkhous, Smith, and Warner[14]	4	Extract of alfalfa	Human bile and sodium taurocholate	Prothrombin returned to normal in each case
Butt, Snell, and Osterberg[15] Snell, Butt, and Osterberg[73] Butt, Snell, and Osterberg[16]	17*	Extracts of fish meal and alfalfa	Animal bile salts of several varieties	Prothrombin was controlled in 15 instances; 2 patients died with hemorrhage; some vitamin K was given intramuscularly
Dam and Glavind[22] Dam and Glavind[25]	5	Extract of alfalfa	0	Blood coagulability by the method of these authors returned to normal in all cases
Quick[61]	1	Alfalfa	?	Ineffective

*These authors treated 60 patients with obstructive jaundice. How many of these were treated prophylactically without a prothrombin deficiency is not stated. From cases cited, it is evident that at least 17 cases treated had a prothrombin deficiency.

Fourteen additional cases of prothrombin deficiency in jaundiced patients studied in the Harrison Department of Surgical Research are presented. These patients were treated in four Philadelphia hospitals. Details of the therapy used and the results obtained are given in Table III. The prothrombin times were determined according to the method of Quick[58, 62] and for the sake of uniformity are recorded with reference to the normal controls.

The source of vitamin K was a preparation of dried young cereal plants (oats and wheat) made by the Cerophyl Laboratories, of Kansas City, Mo., and marketed under the name of cerophyl. This preparation has been assayed by Elvehjem,[33] who found that it would protect chicks when added to a K-free diet in the proportion of 1:400. It is a greenish powder easily ingested in capsules or in tablet form. It can also be taken as a powder shaken up in fruit juice or tomato juice. It contains several other vitamins and consequently is not

adapted for experimental work in which it is important to exclude the effects of vitamins A, B_1, B_2, and C.

The four bile salt preparations used, desicol, bilron, decholin, and sodium deoxycholate, all appear to be effective in appropriate dosage. Sodium deoxycholate is probably the most effective per unit of weight.

Except for the case mentioned by Quick[61] and two cases mentioned by Butt, Snell, and Osterberg,[16] all previously reported cases of prothrombin deficiency treated with vitamin K have responded satisfactorily. In our first patient (O. S.) the cause of failure was probably an insufficient dose of bile salts. In the case of R. P. vomiting and poor cooperation in taking the vitamin preparation undoubtedly resulted in a smaller net intake than the amount ordered. In the case of E. W. we have been unable to explain the poor response. It is possible that with a pure injectable preparation of vitamin K more uniform results might be obtained. In none of our patients, however, has serious hemorrhage occurred.

The mode of action of vitamin K has not been fully explained. The presumption, of course, is that it is a necessary building stone for the formation of prothrombin. This latter material, however, has never been isolated and like complement is known only by its function. In fact, it was thought for a time that the two might be identical, but they were differentiated by their reaction to aluminum hydroxide (Quick[56]) and to toluidine blue (Wising[84]).

Certain types of liver poisons produce a prothrombin deficiency. Smith, Warner, and Brinkhous[71] reported that chloroform anesthesia would reduce the prothrombin concentration in dogs very markedly within twelve hours. This has been confirmed by Quick[61] and in studies being made in this department. Similar results are said to follow the administration of phosphorus[82] and carbon tetrachloride.[61] Ether anesthesia is said to be without effect.[26]

Another method of producing a prothrombin deficiency is to feed animals spoiled clover hay. The hemorrhagic disease resulting from ingestion of this material is known among veterinarians as sweet clover disease and the nature of the dyscrasia was demonstrated by Roderick.[68] It is readily cured by feeding alfalfa, though it is doubtful whether this is due to the vitamin K content of the latter as Quick[59] found it to be effective even after ether extraction.

Recent investigations of the mode of action of vitamin K have been reported by Dam and co-workers.[26] They showed that K in highly concentrated form did not contribute in vitro to coagulability of blood or plasma from K-avitaminotic chicks even after contact for considerable periods. They were able to show that removal of the spleen did not alter the response of K-avitaminotic birds to the vitamin. The unexpected finding that exclusion of the liver from the circulation (in geese) was followed by improved blood coagulability according

TABLE III

RESULTS OF THE TREATMENT OF PATIENTS WITH PROTHROMBIN DEFICIENCY BY CEROPHYL (VITAMIN K) AND BILE SALTS

HARRISON DEPARTMENT OF SURGICAL RESEARCH

PATIENT AND DIAGNOSIS	PROLONGATION PROTHROMBIN TIME BEFORE TREATMENT (% OF NORMAL)	THERAPY	PROLONGATION PROTHROMBIN TIME AFTER TREATMENT (% OF NORMAL)	RESULT
O. S. Carcinoma of pancreas	4,000	Cerophyl, 5.0 gm. Desicol, 1.0 gm. } daily for 2 days, then Cerophyl, 25.0 gm. Desicol, 3.0 gm. } daily for 5 days Transfusion	4,000	Hemorrhage into a biopsy wound Patient died
S. L. Carcinoma involving common duct	300	Cerophyl, 7.0 gm. Bilron, 2.0 gm. } daily for 3 days Transfusion, cholecystgastrostomy Cerophyl, 7.0 gm. Bilron, 2.0 gm. } daily for 6 days	200 Normal	Recovered No hemorrhage
P. S. Common duct obstruction due to stone	30	Cerophyl, 15.0 gm. Decholin, 2.0 gm. } daily for 5 days	Normal	Operated upon No hemorrhage
N K. Common duct obstruction Small hemorrhage	40	Cerophyl, 15.0 gm. Decholin, 4.0 gm. or Bilron, 2.0 gm. } daily for 5 days	Normal	A slight hemorrhage had occurred after choledochostomy
After K was stopped, fresh bleeding occurred	30	Cerophyl, 15.0 gm. Decholin, 2.0 gm. } daily for 6 days	Normal	No further hemorrhage

TABLE III—CONT'D

I. P. Liver abscesses Ulcerative colitis	80	Cerophyl, 15.0 gm. Bilron, 2.0 gm. } daily for 3 days followed by a few smaller doses of sodium deoxycholate	30	No hemorrhagic phenomena; vomiting made the administration uncertain
E. W. Catarrhal jaundice	60	Cerophyl, 15.0 gm. Bilron, 2.0 gm. } daily for 3 days	60	Recovered without hemorrhagic phenomena; the vitamin appeared to have no effect
G. Z. Stricture of common duct; slight hemorrhage on eighth postoperative day	40	Cerophyl, 15.0 gm. Bilron, 2.0 gm. } daily for 9 days	Normal	No further hemorrhage
K. G. Obstructive jaundice	40	Cerophyl, 15.0 gm. Bilron, 2.0 gm. } daily for 6 days	Normal	No hemorrhagic phenomena; operation refused
R. P. Obstructive jaundice	150	Cerophyl, 15.0 gm. Sodium deoxycholate, 0.6 gm. } daily for 5 days	150	No hemorrhagic phenomena; operation refused
P. Obstructive jaundice	30	Cerophyl, 15.0 gm. Sodium deoxycholate, 0.6 gm. } daily for 7 days	Normal	No hemorrhagic phenomena
N. Obstructive jaundice	60	Cerophyl, 15.0 gm. Bilron, 2.0 gm. } daily for 1 day	50	Operated upon 2 days later; no postoperative hemorrhage
S. Obstructive jaundice	30	Cerophyl, 7.5 gm. Bilron, 2.0 gm. } daily for 10 days	Normal	No hemorrhagic phenomena
S. Biliary fistula	1,200	Cerophyl, 10.0 gm. Bilron, 2.6 gm. } daily for 3 days	Normal	Patient was bleeding from ears and gums before treatment
Baby K. Hemorrhagic disease of the newborn	600	Cerophyl, 2.5 gm. Bilron, 0.6 gm. } daily for 1½ days	Normal	Patient had been bleeding from cord and nose 24 hr. before first prothrombin determination but bleeding stopped following a transfusion given before these determinations.

to the method of Schønheyder[70] prevented a satisfactory evaluation of the role of the liver. The increased coagulability was attributed to a decrease in antithrombin.

Partial hepatectomy carried out by Warner[80] resulted in a decrease in prothrombin concentration which could be correlated to some extent with the amount of liver removed.

The present hypothesis on the relation of vitamin K to the hemorrhagic tendency in jaundice may be summarized as follows: The hemorrhagic tendency in jaundice is due to a deficiency in plasma prothrombin which in turn is due to a K avitaminosis which in turn results from absence of bile salts from the intestinal tract. Absence of bile salts may occur without obstruction of the common duct for it has been repeatedly shown that bile from the liver after obstruction may contain no bile salts and that these salts may not reappear in the bile until many days after the obstruction has been relieved.[65, 77] Prolonged clotting time has been observed by Walters[78] in a patient with carcinoma of the liver who showed no jaundice and it seems probable that a prothrombin deficiency will be found in certain patients with liver injury of various types not associated with jaundice. Patients with complete biliary fistulas may develop a hemorrhagic diathesis and a prothrombin deficiency[81] even though they show no jaundice. Whether the liver damage which occurs in obstructive jaundice decreases prothrombin directly or whether it does so solely through its effect on bile salts is an unproved point. Of course, the evidence that the liver is the chief source of prothrombin is not complete though the recent paper of Warner[80] strongly supports this contention.

Two sets of observations indicate that the absence of bile salts in the intestinal tract may not be the sole factor in producing the prothrombin deficiency. One is the fact that doses of vitamin K and bile salts adequate to correct a prothrombin deficiency promptly in most instances may have very little effect in an exceptional case (Table III, Case E. W.). The other is the fact that, although bile fistula dogs in which no bile gains access to the intestinal tract require two to three months to develop a prothrombin deficiency, dogs receiving liver poisons, such as chloroform anesthesia, develop such a deficiency in a few hours.

Hepatic damage incident to the use of anesthetics in general use has been shown by Rosenthal and Bourne,[69] using the bromsulphthalein test, and more recently by Boyce,[13] using the hippuric acid conjugation test of Quick, and by Gray, Butsch, and McGowan[37] in common duct cases, using the bile salt concentration of hepatic bile as the indicator. The results of the latter two studies are substantially at variance, but both studies show that demonstrable hepatic injury can follow anesthesia. It is noteworthy that in the report by Boyce,

which showed substantial injury with spinal anesthesia, the blood pressure was not controlled so that liver anoxemia may have developed. Goldschmidt, Raydin, and Lucké[36] have shown that severe liver injury may even follow ether anesthesia if liver anoxia occurs.

On the basis of the data available, it is not possible to establish the mechanism of the action of vitamin K in detail. It appears probable that the amount of vitamin absorbed is not the only factor that may result in a prothrombin deficiency but that liver damage from various causes may do so also. Furthermore, Lichtman and Chambers[49] have described a sterol fraction of hog liver fat which has the power of curing the hemorrhagic disease of chicks but which differs chemically from K. Until confirmation of this work appears, it is difficult to evaluate this finding.*

SUMMARY

It now seems certain that the hemorrhagic tendency in jaundice is associated with a decrease in plasma prothrombin and that vitamin K when administered orally with bile salts is usually effective in correcting it.

The best test for the hemorrhagic tendency in jaundice is prothrombin determination by one of the methods using an excess of thromboplastin. The method of Quick,[58, 61] while perhaps not the most exact, is probably the most practical for the clinical laboratory.

All patients with obstructive jaundice should have prothrombin determinations performed before operation. Operation should be deferred, if possible, if the prothrombin concentration is decreased.

Usually the oral administration of vitamin K and bile salts will restore prothrombin deficiencies to normal in a few days. The occasional case will respond less satisfactorily, but whenever possible the drugs should be continued, if necessary in increased dosage, until the prothrombin concentration has returned to normal.

In the presence of actual hemorrhage or if operation must be performed in the presence of a low prothrombin concentration, fresh blood transfusions may be relied upon to supply prothrombin directly.[61] Blood from "blood banks" is not recommended because its prothrombin content is usually decreased.[67] The prothrombin concentration may fall rapidly in the postoperative period[16] and for this reason it is wise to follow it closely during this time.

As vitamin K therapy is inexpensive, it is probable that it will be used routinely in patients with obstructive jaundice both before and after operation even though no prothrombin deficiency is found. By

*Almquist and Klose (J. Am. Chem. Soc. **61**: 745, 1939) recently have reported a combination of a potent preparation of vitamin K with deoxycholic acid. When this combination is broken down, the resulting product appears to be highly purified but does not have the characteristics of the crystals with vitamin K potency reported by Thayer et al.[71] It appears possible therefore that K is not a single substance but a group of substances with the same activity.

this means the frequency with which indications for transfusion arise may be reduced.

Routine administration of vitamin K does not as yet avoid the necessity of prothrombin determinations as the response to the oral administration of vitamin K and bile salt is not uniform.

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Book Reviews

Plastic Surgery. By Arthur J. Barskey, M.D., Beth Israel Hospital, New York City. Cloth. Pp. 355, with 432 illustrations. Philadelphia, 1938, W. B. Saunders Company. $5.75.

This small monograph on plastic methods in surgery is an eminently practical book. In 355 pages, profusely illustrated with suitable drawings and photographs, the author discusses the phases of surgery which fall within the special province of plastic surgeons. The principles involved in the use of free skin grafts, flaps, and pedicles are discussed well. The transfer of fascia and its practical applications is well done. However, no mention of its use in hernia operations is made.

The author prefers the classification of Veau to that of Davis and Ritchie in clefts of the lip and palate. The author uses also the somewhat unanatomic designation of harelip. In connection with the discussion of lipectomy, no mention is made of lipemia which attends operation occasionally or the danger of embolism.

Plastic operations upon the bowel, penis and scrotum, undescended testis, and kidney pelvis are not discussed.

There is one chapter on restorative aspects of orthopedic surgery and concluding chapter on prostheses. Well-selected bibliographies accompany each chapter.

The book can be recommended highly as a useful and practical text.

Anus, Rectum and Sigmoid Colon. By Harry E. Bacon, M.D., Temple University, Philadelphia, Pa. Cloth. Pp. 600, with 487 illustrations. Philadelphia, Pa., 1938, Lippincott Company. $8.50.

The author's object in writing this text has been "to place within the reach of all divisions of the medical profession a comprehensive and readily intelligible exposition of our present knowledge of the various affections of the anus, rectum and sigmoid colon." In his introductory foreword Lockhart-Mummery, of London, states: "Medical text-books are of two kinds. Those which express the opinions of a single man and those which more closely resemble an encyclopedia and give a comprehensive survey of all views. . . ." Whereas the author of this text does speak out of his own experience, he has followed his objective quite closely and has chosen to summarize the opinions of men whose statement is believed to be authoritative. In the main, the author has done this well; there are times, however, when the author details one opinion after another, so superficial in concept that entire omission of these shallow notions would have spared the reader needless irritation. Authors owe something to their readers in not repeating everything they hear or see.

The alleged causes of hemorrhoids enumerated are really ridiculous, yet the author does not deem the upright position important enough an etiologic agent to mention it.

The author's treatment of the surgical aspects of cancer of the pelvic colon and rectum is unusually well done and these chapters are also very well illustrated. A comprehensive list of references follows each chapter. The orderly plan in which the subject matter is discussed will find favor with readers. There is much to praise in this splendid volume and little to criticize.

The lymph follicles have probably more to do with the origin of cryptitis than the author allows. He believes that establishing colostomy on the lower portion of the pelvic colon will eliminate prolapse, when, as a matter of fact, prolapse may concern the proximal or distal loop of the colostomy. The author favors the operation of presacral neurectomy for congenital megacolon; whereas, those who have had the most experience with sympathectomy for Hirschsprung's disease feel that it is inadequate. The author unfortunately omits all discussion of the items of diverticulae of the pelvic colon and acute obstruction due to malignancy, rather serious omissions in a book which essays to treat of the diseases of the sigmoid colon. The favorite prescriptions of well-known proctologists which occupy many pages could better have gone without mention.

Despite the failings that have been referred to, this text is without question one of the better books written by proctologic surgeons within recent years. It should prove valuable as a source book to general practitioners, surgeons, and proctologists.

Röntgendiagnostik der gelenke mittels doppelkontrastmethods. By J. Oberholzer, M.D., Bircher's Clinic, Aarau, Switzerland. Paper. Pp. 128, with 134 illustrations. Leipzig, 1938, Georg Thieme. Rm. 23.

Kleinberg advocated inflation of joints with oxygen as early as 1921 for roentgen study. The method, however, has not had an important vogue in this country. The author, who writes from Bircher's Clinic in Aarau, Switzerland, lends the very definite impression that the injection of negative (gaseous) as well as positive (opaque) media into joints for diagnostic purposes enjoys wide usage throughout continental Europe. The author says in his introduction that in Bircher's Clinic alone more than 2,000 joint injections have been made during the last eight years.

From the illustrations shown, one would infer reasonably that the method has real value, particularly in demonstrating objectively internal derangement of the knee joint, such as a torn meniscus or severed cruciate ligaments. The author says he could not inject the hip joint successfully on the cadaver for roentgen purposes, but finds it a feasible procedure in the living patient.

Anyone interested in improving diagnostic accuracy in joint disease will find this little monograph helpful.

Spinal Anesthesia. By Louis H. Maxson. Foreword by W. Wayne Babcock. Cloth. Pp. 409, with 69 illustrations. Philadelphia, 1938, J. B. Lippincott Company. $6.50.

Medical literature is already overcrowded with references to spinal anesthesia; nevertheless, a justifiable contribution is made by Maxson (1) in offering a good exposition of the principles upon which good practice must be based; and (2) in describing a variety of techniques, followed by his own experience and critical judgment.

It is unfortunate that the untimely death of the author in October of the year of publication has deprived medical literature of further contributions from his pen.

The book reviews fairly thoroughly the history of spinal anesthesia, beginning in 1891 up to the present time. It describes in detail many of the different means of control of the anesthetic agent, when it is injected into the spinal canal.

His description of the anatomy involved in spinal anesthesia is considered from a practical viewpoint. Any doctor of medicine would not waste his time by

reviewing this chapter many times. An anesthetist should make himself so familiar with this chapter that he should have it flash through his mind each time he proposes to do a spinal anesthesia.

The physical laws involved in the technique and the physiology of the nervous system are also well discussed. The practical consideration of these points cannot be overlooked by the anesthetist who intends to have success in spinal anesthesia.

A large portion of the book reviews the drugs and techniques of the author and many other anesthetists, and describes in a new concise manner their agent, technique, and the results. The author usually gives his comment at the end of each description.

If the description of degrees of respiratory depression and the treatment of such depression, as described on page 210 and following, were intimately familiar to every practicing physician, many unnecessary deaths occurring from other causes than spinal anesthesia might be prevented.

The failures, difficulties, dangers, complications and sequelae, advantages and disadvantages, indications and contraindications for spinal anesthesia are well presented. The author's comments and the quoted comments of other anesthetists are well worth reviewing.

For the beginner, it is a book from which he would gain considerable knowledge of the subject. For the experienced anesthetist, the book is a very good though incomplete compilation of the literature on spinal anesthesia. It is to be highly recommended for anyone doing spinal anesthesia.

Diagnostik und therapeutische Indikationsstellung bei den chirurgischen Erkrankungen der Harnorgane. By Professor Dr. Peter Janssen, Dusseldorf. Paper. Pp. 316. Berlin, 1938, Julius Springer, Publishers. R.M. 15.

As the author states in the preface, this book is intended as a guide to clinical urology largely for the use of the student and the general practitioner, and the book serves the intended purpose very well. In no sense should it be regarded as a comprehensive treatise on the subject of urology, but as a guide to the clinical application. Its practical nature is illustrated even in the pages devoted to anatomy of the various portions of the urinary tract, which are written with a view to clinical and therapeutic application. The discussions of diagnostic methods employed are excellent and are very evidently based on wide experience.

Among the best chapters are those devoted to injuries of the urethra and bladder. They are apparently based on the experience which the author obtained in the World War and in industrial surgery. A thorough description of the pathologic complications and treatment of these lesions is included.

The book illustrates the differences in opinion held by American and German urologists concerning some of the lesions observed in the urinary tract. Viewed from a therapeutic and surgical standpoint, many of the observations are hardly up to the standards set by American urology. The discussion of the treatment of urinary infection does not include all recent developments and no mention is made of modern chemotherapy and its various ramifications. The author fails to mention transurethral drainage of abscesses involving the prostatic ducts. He does not mention the grading of tumors of the bladder. In the treatment of tumors of the bladder, transurethral methods and cystectomy are not discussed. He regards the treatment of diverticula of the bladder as being always surgical and fails to recognize the fact that transurethral removal of obstruction of the bladder neck will suffice in most cases to overcome the diverticulum.

He still estimates renal function by means of urinary cryoscopy, Volhard's concentration test, and phloridzin. He fails to mention the phenolsulfonphthalein tests or the retention of urea and urographic visualization. He prefers transvesical (retrograde) pyelography to excretory urography. He gives the latter procedure but limited value and importance and apparently does not rely upon it as final in any case. He speaks of the frequent occurrence of vesical stones in children. This may be true in Europe, but it is not true in the United States.

Owing to the limitation of scope and space, many important clinical and pathologic conditions are briefly dismissed. In the discussion of perinephritic abscess the author does not mention the roentgenographic and urographic data. In the discussion of renal tumor he distinguishes between renal carcinoma and hypernephroma and regards them as different pathologic entities. He refers to hypernephroma as the tumor of Grawitz, which has its origin in adrenal rests. He believes that trauma is probably a definite etiologic factor in cases of tuberculosis of the kidney and genitals.

Although not an outstanding contribution to urologic literature, taken as a whole the volume is very readable and contains much which should be of value to the student and to the general practitioner.

The Rockefeller Foundation International Health Division Annual Report, 1937. Paper. Pp. 243, New York, 1938, Rockefeller Foundation.

This is the report of the stewardship of an income of some two and one-half million dollars which were spent in the promotion of public health. The first section is a collection of brief abstracts of scientific studies of the epidemiology of infectious diseases, especially of yellow fever and malaria. Here are to be found résumés of certain studies of virus diseases, a field in which the Rockefeller staff has made some of the most outstanding contributions of recent years. Perusal of these abstracts will give the reader a good concept of the important developments in this field and their application to the control of these diseases. No other research group has contributed so much to the knowledge of virus diseases. The second section outlines the results of the grants in aid to health departments in many countries widely scattered throughout the four corners of the globe. These grants were designed to supplement local funds in the establishment of essential facilities which would later be incorporated as an integral part of the public health structure of the community to which the grants had been made. The third part of the report deals with the aid given to the training of professional personnel for public health service. Since its establishment in 1913, the International Health Division of the Rockefeller Foundation has become well known in both professional and lay circles. Yet few who have not read a report of a year's work of this organization can fully appreciate the vital part that it has played and still occupies in the promotion of medical science and the application of these findings to the solution of community problems.